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Public Health

SILVER, G. A. **Beyond General Practice: the Health Team.** *Yale J. Biol. & Med.* 1958, Sept., v. 31, No. 1, 29–39. [34 refs.]

This is an interesting article in which the author examines in some detail the present status of the general medical practitioner in the United States which has changed so greatly in the last 50 years or so. "The general practitioner who knew a community inside and out, who encompassed all existing medical knowledge and skills, who was able to diagnose and minister to physical and emotional illness—from medical training partly, but more from intimate association with the people he ministered to—became obsolescent at the turn of the century." His position has been changed by the scientific advances in medical knowledge which make it impossible for one individual "to encompass the whole of medical knowledge and skill"; reformulation of medical education on a scientific basis; the "transformations in American social life" from "mechanization, industrialization, urbanization, and depersonalization"; and the "internal revolution of medical care". It is not possible, in the view of the author, to restore the medical practitioner's position; "rather, a new and more realistic format for the provision of medical services which were formerly the general practitioner's responsibility is needed and such a program is here described". General practice "is neither attractive to physicians nor lucrative, nor by present standards adequate to the needs of patients" and the problem that thus exists may perhaps have various solutions. Group practice is one obvious solution under certain conditions. A "wholly new type of family medical practice postulated here to fill the gap left by the disappearing general practitioner" is fully described and discussed. In this scheme "Preventive and therapeutic services are provided by a 'health team' composed of a physician trained in internal medicine, a psychiatric social worker, and a public health nurse. For children under 13, the evaluation, medical care, and preventive responsibility are lodged in a trained pediatrician". The health team is supported by 2 consultant bodies and is also advised by a group of consultants comprising a psychiatrist, psychologist, health educator, and social scientist.

This proposed health team is part of a health programme set up under the joint auspices of the Community Service Society, the Columbia College of Physicians and Surgeons, and the Montefiore Hospital, New York City. *M. E. Delafield*

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. NO. 156. **Expert Committee on Training of Health Personnel in Health Education of the Public.** Report. Geneva, 28 October–1 November 1957. 40 pp. [Refs. in footnotes.] 1958. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr. 1.–.]

The Expert Committee on Training of Health Personnel in Health Education of the Public was set up by the Ninth World Health Assembly held in May 1956. Its meeting was held from 28 October to 1 November 1957. The collective views of the international group of experts who composed the Committee are presented in this report. In the introduction "the Committee recognizes that the need for preparing health workers in health education exists in all countries" but no "standard" training programme can be laid down and "Each country must formulate its own plans according to its particular needs, resources, and available technical services." The sections of the report cover: needs for training in health education; the objectives of training; health workers for whom training in health education is necessary; the scope of health training opportunities; the role of various workers in health education; planning, organization, and conduct of health education training and further studies. In an appendix it is stated that "the Committee discussed whether the existing evidence showed that health education, skilfully carried out, was effective in reducing or preventing ill-health". Reference was made to 6 papers on this question.

The views of the Committee are set out fully and clearly with suggestions and criticisms.

M. E. Delafield

Maternal and Child Health

MEDALIE, M. **Cyanosis in Infancy. An Outbreak of Methaemoglobinaemia in a Nursery.** *Med. Proc.* Johannesburg. 1959, Jan. 24, v. 5, No. 2, 31–7. [21 refs.]

In this paper an account of an outbreak of cyanosis in infants in a maternity block of a country hospital is preceded by an outline of the mechanism and causation of cyanosis with some clinical and pathological particulars. There were 4 infants who were acutely ill with cyanosis, rapid respiration and pulse rates but no temperature. A day later 2 further cases developed. The age of the infants ranged from 1 to 20 days. A likely diagnosis was methaemoglobinaemia and investigation showed that napkins freshly marked in large print with ink containing aniline were being used. There was a strong aromatic odour in the ward. Methylene blue in watery solution (a dose of 2·0 cc., containing 6·0 mgm. of the dye) was given intravenously to the first 4 infants with dramatic effect for the cyanosis disappeared completely in about 45 minutes.

The history, chemical causes, mechanism, symptoms and treatment of methaemoglobinaemia are discussed.

M. E. Delafield

HORNER, T. & HICKLING, S. **Lead Poisoning of Unusual Origin in Two Children.** *New Zealand Med. J.* 1958, Dec., v. 57, No. 322, 600–604, 1 fig. on pl.

"In most countries, including New Zealand, lead poisoning in childhood cannot be described as a common disease, nor yet is it excessively rare." During the last 10 years 49 children under 15 years of age have been admitted to hospitals in New Zealand suffering from lead poisoning.

A boy aged 5 years was taken to the doctor by his mother with symptoms of morning vomiting, constipation and lassitude. Examination of the blood gave a picture of low red cell count, haemoglobin 9·6 gm. and 30,000 stippled cells per million red cells. Diagnosis of lead intoxication was confirmed by X-ray which showed marked lead lines in the lower limbs. Investigation of the family of the child revealed that a sister, though without symptoms, was also a case of lead absorption. Both children made a good recovery in hospital where they were treated with calcium disodium versenate.

The investigation of the source of the lead is fully described. A number of possibilities were examined with negative results but ultimately it was found that the lead was derived from the glaze on an ornamental "coloured artware" jug in which a lemon cordial with a citric acid base was kept. In an analysis of the cordial after standing in the jug for 18 hours a lead content of 400 parts per million was found.

M. E. Delafield

Health of Nurses, Students and Hospital Staffs

BECKETT, M. B. & TUPPER, C. J. **The Responsibility of a University Administration for Health of Students and Faculty.** *Amer. J. Pub. Health.* 1959, Jan., v. 49, No. 1, 70–5.

In this article the authors discuss the rate at which interest in the health of students has developed in colleges and universities in the United States. Although most of these educational institutions recognize the importance of this interest nevertheless "Programs and acceptance of responsibility for health care of students vary from practically nothing, or not more than providing first-aid packages, to services including specialists and elaborate equipment". The University of Michigan has found it necessary and feasible to provide a considerable degree of specialized service. "To provide total care without cost to the student would be inordinately expensive" and in conditions of long standing "probably not a direct responsibility of the school" but it is the policy of the University to provide special investigations at as low a cost as possible. Infirmary care for convalescence after acute upper respiratory infections or gastro-intestinal upsets is a necessary provision for students who are living away from home. The provision of full hospital care is probably best arranged through some form of medical insurance plan with free choice of a physician when the care needed is "beyond or out of the jurisdiction of the health service". There is mention of the value of a health service as a medium for health education.

In addition to organizing a health service for students the University recognizes its responsibility for the health of employees and faculty members. There is a description of the programme which started in 1956 for the detailed specialist investigations which were made available. By 1958 almost 500 faculty members had been examined and the first 294 of these were professors ranging in age from 43 to 87 years.

"A final summary of the 294 patients examined revealed a total of 387 previously known significant defects but 465 previously unknown significant defects."

M. E. Delafield

Care of Old Persons and the Chronically Ill

PERROW, C. **Research in a Home Care Program.** *Amer. J. Pub. Health.* 1959, Jan., v. 49, No. 1, 34–44.

The inherent difficulties of assessing the results of home care are very great but there is a need for ascertaining the amount of success attained. Controlled trials are not a practical possibility for many reasons, the chief of which is that of matching patients, comparable diagnoses in the same diagnostic group are not easy to find, and a much larger number of patients than home care programmes have or could at present handle would be necessary to control the large number of variables successfully. The present paper is a description of the methods used in the San Francisco Home Care Program to judge their results. The condition of every patient receiving home care was assessed and the possible condition on discharge was estimated. The condition on discharge was grouped into 4 categories, full ambulation, partial ambulation, self care and palliative. All members of the staff who came in contact with the patient were asked what they thought the patient could achieve. The assessment of the patient's possible achievement differed between the groups composing the team, physicians, nurses, social workers and physical therapist, and within the groups of workers. The patient's attitude was also assessed and placed into 3 categories and the team found that this was also difficult to judge. The attitude of the patient could be influenced by his family and by the home care team.

This type of enquiry is full of ambiguities but it does give some measure of the results attained when a control trial is not possible and although the results may not be of general application they would give valuable guidance to the team of workers concerned.

W. J. Martin

Vital Statistics and Epidemiology

MAGDELAINE, M. Recherches sur la clientèle hospitalière. [**Survey of Hospital Patients**] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1958, Sept., Oct.–Nov. & Dec., v. 6, Nos. 6, 7 & 8, 539–605; 651–720; 865–87, 64 diagrams. [31 refs.]

The patients in this enquiry were those of the Hôtel-Dieu in Paris, and were drawn from the district of the Seine with a population of almost 4 millions but almost 90% of the admissions were from Paris The enquiry was undertaken in 2 parts, 1952–4 and 1954–5, and during these 4 years almost 6,000 patients were admitted to the hospital, slightly more than one-half of them were males. For each patient a 4-page questionnaire was completed, this dealt mainly with the social-economic background of the patient, the method of entry and discharge, length of stay in hospital and the diagnosis. The results of this investigation have been written mainly from the social-economic-administrative aspect. Persons aged 60 years or more formed one-sixth of the general population and accounted for one-third of the patients and occupied one-half of the beds. The rate of admission per 10,000 population rose steadily with increasing age from 39 at ages 15–19 to 767 at ages 80 and over, with the exception of ages 20–29 which had a rate in excess of that at ages 30–39. The length of stay in hospital has been set out in great detail for the 1954–5 enquiry. Durations of under one week formed 30% and durations of over one month 29% of all durations in hospital. Males had a much longer average stay in hospital than females up to the age of 70 years but after this age the females had the longer duration. The most frequent length of stay was one day, the median stay was 16 days and the mean stay was 30·5 days and the longest duration was 866 days. During the 2 years 20% of the males and 19·5% of the females had more than one period in hospital. The circumstances of the admissions to hospital are tabulated in detail, whether emergency, out-patient etc., and age, sex and month of admission. The discharges are also shown by age, sex and the various reasons for leaving hospital.

The social-economic condition of the patient was studied and the tabulations included the age, sex, civil state, position in family, number of generations living together, housing and overcrowding which was divided into groups from very good to very bad, whether patient was employed or not, financial state which is given in 4 qualitative groups. 22% of the patients lived in overcrowded conditions classified as bad or very bad and the housing of 45% was bad or very bad. About one-half of the patients were employed. The finances of 34% were considered to be inadequate and 35% had no resources.

The morbidity has been grouped according to the international classification and the cases of multi-diagnosis are discussed, over one-third of the patients had several complaints. The most frequent diagnoses were respiratory diseases, tuberculosis, cancer, alcoholism, mental disease. In 1954–5 objection to post-mortem was made in 27% of the deaths. The deaths are shown by cause in tabular and diagrammatic form.

The author discusses administration problems, the difficulties of multidiagnosis, the importance of the social background of the patient and the effect of social and family worries and stresses the need for better understanding of the social-medical needs of the patient. He concludes that research should be continued in order that "in our role of doctor we may be able to adapt ourselves to the needs of the patients confided to our care in hospital". *W. J. Martin*

DREYER, Karen & FRANDSEN, Erna. **Medico-Statistical Information from Denmark for the Years 1956 and 1957.** *Danish Med. Bull.* 1959, Jan., v. 6, No. 1, 26–32, 1 fig.

This paper is an extensive summary of the information relating to the health of Denmark during 1956 and 1957. In Denmark there were, in 1957, a practising physician for every 864 persons, a practising dentist for 2,030, dentist with own practice for 3,143, one pharmacy for 12,725 persons and a practising midwife for 1,567 women in the age-group 15–49 years. The number of cases of notifiable diseases in 1957 was 1,125,385 compared with 716,771 in 1956. The large rise was mainly due to the outbreak of influenza with 544,613 cases which were 429,410 more than in 1956. The percentage distribution of influenza was 36% under 15 years, 59% at ages 15–64 and only 5% at ages over 65. The influenza fatality rate among persons aged 65 and over was slightly over 10 per 1,000, for infants it was 1·02 and in childhood and young adult life it varied from 0·10 to 0·38. The numerically most important of the 33 conditions which were notifiable were influenza, angina and tonsillitis, tracheobronchitis, whooping cough, enteritis, and measles. No case of diphtheria was notified in either year. The fall in the death-rate in Denmark has followed a similar pattern to that in England and Wales, a very large decline in the younger ages, a smaller decrease in late middle life and only a small improvement in old age, and the female rate has declined faster than the male. The deaths are shown for 50 causes. The death-rate in 1957 was 930 per 100,000 population and slightly more than one-half of this rate was contributed by 3 causes, 227 for arteriosclerotic and degenerative heart diseases, 201 for malignant neoplasms and 118 for vascular lesions of the central nervous system. Notifications of pulmonary tuberculosis in 1956 numbered 609 for males and 518 for females, 2/5 of the females were aged 25–44 and 1/3 of the males were aged 45–64.

The hospital accommodation in 1956 comprised 145 hospitals with 25,938 beds and a further 19,411 beds were available in 168 special institutions, making an average of 10 beds per 1,000 population. The number of admittances to hospital are shown for 26 main diagnoses, about half a million cases were admitted during 1956. The number of bed days was 8·8 million and the average length of stay was 18 days. Diseases of the digestive system were the cause of the largest number of admissions. The number of admissions, beds and average stay in hospital are given for 18 hospital departments. *W. J. Martin*

FRISK, A. R., WERKÖ, L., HOLMGREN, A. & STRÖM, G. **Stockholm's City Health Survey 1954.** *Acta Med. Scandinavica.* 1959, Feb. 7, v. 163, No. 1, 1–14, 2 figs.

The Health Survey of the City of Stockholm described in this paper was conducted in 1954 with the help of a grant from the City Council. "Its purpose was to examine every individual among a representative selection of the Stockholm population according to a predetermined schedule of diagnostic methods." Some details of this study have already been published [this *Bulletin*, 1958, v. 33, 92, 93].

Invitations to take part in the survey were issued to 3,646 persons over 21 years of age but only 2,504 accepted. Each person who took part completed a "comparatively detailed" statement of health and medical history. This was followed by a complete physical examination; laboratory examinations of blood, urine and faeces; a Wassermann test; electrocardiograms; and X-rays of heart, lungs and stomach. Each case was then discussed at meetings of all the physicians for assessment. The results of the survey are fully described and there are 12 tables of numerical data.

In 479 (20%) persons no morbid condition or abnormality was found but in the remaining 2,025 persons 4,636 diagnoses of morbid conditions were made. Of these diagnoses 472 were graded as "non-essential" and 4,164 were regarded as "essential from the health aspect to a greater or lesser degree". Some 800 of the latter were in persons who were not aware of them but which in about 200 led to hospitalization. Comments are made on the more important conditions which were diagnosed, *e.g.* active pulmonary tuberculosis (33 cases of which 9 were previously unknown), malignant tumours (12 cases of which 7 were new), diabetes (26), secondary anaemia (79), nervous disorders (425), cardiosclerosis (124 patients of whom only 57 were aware of the condition) and elevated blood pressure at a level of above 165 systolic and 95 diastolic (in 17% of the "evaluees").

The value of a well-planned health survey is clear but it is extremely doubtful whether a wide-scale voluntary health survey should be recommended because of the difficulties of obtaining adequate medical staff and also because of the expense of such a scheme.

M. E. Delafield

EDWARDS, Felicity, MCKEOWN, T. & WHITFIELD, A. G. W. **Association between Smoking and Disease in Men over Sixty.** *Lancet.* 1959, Jan. 24, 196–200. [13 refs.]

Smoking histories were obtained from 1,737 men aged 60 and over on the lists of 11 general practitioners, the group being reasonably representative of the general population of men of these ages. Smoking habits related to age show a pronounced decline in the proportion of cigarette smokers. It falls from 55% of the men at ages 60–64 to 22% at ages 85 and above while the pipe smokers correspondingly increase from 12% to 50%. The amount smoked declined with age. The proportion of men not smoking at all shows little variation with age, being consistently about one-quarter

of the total. In relation to social class the proportion of cigarette smokers is relatively high (50%) in social class V (unskilled workers) and relatively low (35%) in social classes I and II (professional and related occupations).

The recorded smoking habits have been studied in relation to the 8 diseases or disabilities which occurred most frequently in these men. No association is apparent with defective hearing, defective vision, coronary artery disease, arthritis or hernia. A positive association is found with chronic bronchitis and peptic ulcer while hypertension was rather lower in cigarette smokers. Examination of the data by age and social class reveals a consistently higher incidence of bronchitis and peptic ulcer in the cigarette smokers in each social class and at each age. The pipe smoker appeared to be free of these risks. On the other hand the effect on hypertension seemed to be common to cigarette and pipe smokers. Pressures in men who had given up smoking were, however, approximately the same as in those who had never smoked, suggesting that the lowering of arterial pressure is a short-term effect.

[For previous studies by the authors see this *Bulletin*, 1958, v. 33, 94, 548.] *A. Bradford Hill*

CANDIOTTI & MOINE, M. Les principales causes de décès en France en 1955–1957. [**Principal Causes of Death in France in 1955–1957**] *Bull. Inst. Nat. Hyg.* Paris. 1958, Oct.–Dec., v. 13, No. 4, 1187–1206, 12 figs.

Slightly more than half a million deaths were registered in France during each of the 3 years 1955–7. Despite the outbreak of influenza in 1957, with 11,714 deaths compared with 4,109 in 1956, the total deaths were 13,353 fewer than in 1956. The chief features of the returns were the continued fall in the number of deaths from tuberculosis, from 13,285 in 1955 to 11,902 in 1957. At the beginning of this century the annual number of deaths from tuberculosis was about 100,000. Cancer deaths are steadily increasing by about 2,000 a year, for the 3 years 1955–7 the number of deaths was 78,021, 79,812 and 82,066, respectively. Alcoholism and cirrhosis of the liver accounted for 17,355 deaths in 1955, 19,920 in 1956 and 19,053 in 1957. The number of deaths from congenital malformations declined from 16,419 in 1955 to 14,920 in 1957. The 35,326 deaths from violence in 1957 were 1,061 more than in 1956 and 2,804 more than in 1955. Deaths from senility and ill-defined causes fell abruptly in 1957 and the 88,924 deaths were almost 10,000 fewer than in either of the 2 preceding years.

Accidents were the most important cause of death in adolescent and young adult males and accounted for 52·5% of all deaths at ages 15–19, 54·1% at ages 20–24 and 44·3% at ages 25–29. Road accidents were responsible for one-half of the male accidental deaths. Among females of these age-groups accidents formed 26·0, 21·3 and 15·7% of all deaths. At all ages in 1955 the number of accidental deaths was 17,611 for males and 8,651 for females. The number of females dying from tuberculosis was less than one-half of the number of males, 4,127 compared with 9,408, in 1955. The number of deaths attributed to cancer in 1955 was 39,673 for males and 39,889 for females.

W. J. Martin

WELLS, H. B., GREENBERG, B. G. & DONNELLY, J. F. **North Carolina Fetal and Neonatal Death Study. I—Study Design and some Preliminary Results.** *Amer. J. Pub. Health.* 1958, Dec., v. 48, No. 12, 1583–95. [21 refs.]

This study based on an 8-page questionnaire which was completed for every birth and stillbirth of 400 gm. or more in 3 teaching hospitals in North Carolina was designed to "promote interest in fetal and neonatal mortality; to encourage study of their causative factors; and to assemble information from which conclusions can be drawn that will enable maternal and child health programs to provide concrete guidance in the reduction of fetal wastage and neonatal deaths". Neonatal deaths in this study cover deaths while in hospital. The 3 hospitals had about 3,600 deliveries a year with 90 stillbirths and 75 neonatal deaths. As might be expected abnormal labours and abnormal condition of infant at birth had a significant influence on the chance of surviving. An analysis of covariance, after adjusting for several covariables, showed that the mother's age and education were highly significant. Birth interval of multiparae and length of the gestation period were highly significant but parity or pre-natal care was not significant.

The authors suggest that further investigation is necessary to determine the differences between the peri-natal deaths and the infants who survive and that the dissimilarities between peri-natal deaths of premature infants and premature survivors should be studied more intensively. *W. J. Martin*

Communicable Diseases

For the bacteriology of these diseases see the section on Bacteriology below. For those communicable diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN

INFECTIVE DISEASES

In this section the abstracts are arranged as far as possible in the following order: General; Diphtheria, Whooping Cough, Streptococcal Infections, Staphylococcal Infections, Measles, Mumps; Chickenpox, Smallpox; Influenza and other Respiratory Infections, Pneumonia; Hepatitis; Mononucleosis; Meningitis, Poliomyelitis and other Enteric Virus Infections; Encephalitis; Enteric Fevers.

WILLIAMS, R. E. O. **Investigations of Staphylococcal Infection acquired in Great Britain's Hospitals.** *Pub. Health Rep.* Wash. 1958, Nov., v. 73, No. 11, 961–70, 2 figs. [39 refs.]

This paper by the Director of the Streptococcus, Staphylococcus and Air Hygiene Laboratory of the Public Health Laboratory Service in England, was read at the National Conference on Hospital-acquired Staphylococcal Diseases held at Atlanta, Ga., U.S.A., in September 1958. It is a general account of experience in this field in Great Britain, in which bacteriophage typing in the author's laboratory has contributed largely to a better understanding of this problem. This kind of study has shown that all coagulase-positive staphylococci are not equally capable of causing hospital infection. Some interesting figures are given in illustration of this. Among 1,131 independent strains examined in 1954–7, 178 had caused epidemics, and 69% of these belonged to 1 of only 7 types. Type 80 had the largest proportion of epidemic strains: whereas this caused 5 or 6 epidemics only in the years 1954–6, it was recovered from 21 in 1957.

After a historical introduction, the paper discusses the prevalence of hospital infection, emphasizing the necessity for keeping a record of the state of all operation wounds, the contamination of wounds in operating theatres, with particular reference to ventilation systems, the sources of infections in wards, both surgical and maternity, the disinfection of bedding, and the treatment of the carrier state. Staphylococci differ in virulence, and a laboratory test for assessing the degree of this would be very helpful. Carriers and infected patients differ in their capacity for dispersal of their organisms, and epidemics are usually due to the introduction into the ward of someone with a high capacity for dispersing a virulent strain. The author does not believe that there is any single and simple solution to this problem. Staphylococcal infection should be treated as an infectious disease, in strict isolation. Beyond this the best safeguard is rigid asepsis: "there are no gadgets and no drugs or vapors that can relieve the people who handle the patients of their perennial responsibility for handling them aseptically".

L. P. Garrod

VOLOVICH, N. I., PEDENKO, A. I., SMERENSKAIA, A. V., GOLODIUK, L. F. & KALUZHSKAIA, B. A. **The Epidemiological Significance of Carriers of Avirulent Diphtheria Bacilli.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 11/12, 1704–9. [Translated from Russian.]

"(1) Our observations show that the prolonged residence of carriers of avirulent *C. diptheriae* in children's communities does not constitute an epidemiological danger.

"(2) The introduction into practice of a method by which the virulence of *C. diptheriae* can be determined *in vitro* enables us to distinguish measures appropriate to carriers of virulent and avirulent organisms.

"(3) The current instruction should prescribe measures only for the segregation of the carrier of virulent organisms."

FLEKSER, S. I. & TSIRLINA, F. G. **Comparative Assessment of Preparations used to treat the Carrier State in Patients convalescing after Diphtheria.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 11/12, 1714–17. [Translated from Russian.]

"(1) Four preparations were used in the treatment of persistent infected carrier state in patients convalescing from diphtheria—chlortetracycline, tetracycline, cetylpyridinium chloride and chloramphenicol. The most effective proved to be chlortetracycline and tetracycline.

"(2) Of a total of 73 patients treated with antibiotics and followed up at home, 13 again showed relapses into the carrier state.

"(3) The presence of a considerable number of patients with chronic lesions of the tonsils and nose among persistent carriers points to the importance of clearing up the pharynx and nasopharynx in the prophylaxis and treatment of the diphtheria carrier."

BALDOVIN, Coralia *et al.* Aspecte din epidemiologia scarlatinei, rolul anginelor si al factorilor de mediu social în întreținerea si declansarea focarelor de scarlatină. [**Epidemiological Aspects of Scarlet Fever. The Rôle of Tonsillitis and of Social Environment Factors in maintaining and developing Scarlet Fever Foci**] *Microbiol., Parazitol. si Epidemiol.* Bucharest. 1958, Jan.–Feb., v. 3, No. 1, 29–35, 2 figs. [12 refs.] English summary.

An epidemic of streptococcal infection occurred in a school in Rumania in 1952. Among a total of 799 pupils at risk 99 developed scarlet fever and 250 suffered from tonsillitis. The first cases appeared in September at the beginning of the term; the incidences of both conditions both increased in a parallel manner to reach a maximum at the beginning of November, with 143 cases of tonsillitis and 48 cases of scarlet fever in the first 10 days. 170 pupils were boarders,

and the incidence of both conditions among them was 3 times as high as the incidence among the day pupils. 4 types were represented among 161 strains of streptococcus isolated during the epidemic; untypable strains (NT) were encountered most frequently, followed by types 3, 2 and 14. *D. J. Bauer*

VASOJEVIC, S., KOSTIC-VUJACIC, A., POPOVIC, J. & DEBELJKOVIC, N. Osvrt na epidemiologiju i profilaksu šarlaha kod dece i omladine za poslednjih pet godina. [**A Review of the Epidemiology and Prophylaxis of Scarlet Fever in Children and Adolescents in the Last Five Years**] *Higijena.* Belgrade. 1958, v. 10, No. 2, 121–31, 5 graphs. French summary.

The annual incidence of scarlet fever in Belgrade has shown peaks at 5–6-year intervals, with 1,207 cases in 1945, 2,340 in 1950 and 3,067 in 1956, compared with less than 1,000 cases in most intervening years. The number of cases treated at home has increased steadily, rising from 25% of 456 and 583 patients in 1952 and 1953 respectively, to 50% in 1956. The case mortality between 1948 and 1950 was 0·2%, and between 1952 and 1956 0·1%. During epidemic years the clinical course of the disease was more severe and complications were more frequent, occurring in 5·6% of cases in 1956 compared with 0·87% in 1955. Young children were rarely affected and the main incidence of the disease occurred in children of school age. Of 4,527 patients treated in hospital 3,467 were admitted within the first 3 days of illness. *D. J. Bauer*

MOGABGAB, W. J. & PELON, W. **An Outbreak of Pharyngitis due to Tetracycline-Resistant Group A, Type 12 Streptococci.** *J. Dis. Children.* Chicago. 1958, Dec., v. 96, No. 6, 696–8. [12 refs.]

This article from New Orleans gives a warning against the use of tetracycline drugs for the prophylaxis or treatment of group A streptococcal infections without testing for sensitivity. A family outbreak of pharyngitis due to tetracycline-resistant type 12 group A streptococci occurred one week after a member of the family had been treated for a similar illness with tetracycline. In addition, 38 out of 131 throat swabs taken from pupils in a nearby school, some of whom were from the affected family and a family in which a similar illness had been treated unsuccessfully with tetracycline, were positive for type 12 tetracycline-resistant streptococci.

Group A streptococci can easily be made resistant to the tetracyclines *in vitro,* and the common use of these drugs is therefore likely to foster such resistance. It has been customary to omit drug sensitivity tests in the case of streptococcal infections, but where treatment with sulphonamides or tetracyclines is contemplated for group A streptococcal infections, sensitivity tests would now seem to be indicated.

H. Stanley Banks

DONCHEV, D., STOIANOVA, M., GRIGOROVA, M., BALKANSKA, V., NENKOVA, V. & DUMANOVA, S. **Parapertussis in Kindergartens and Nurseries in Sofia.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 5, 732–9. [Translated from Russian.]

There have not been many investigations of parapertussis on the scale described in this article, and it is interesting to have confirmation of general views on the subject, which have not hitherto been very firmly based.

Parapertussis is a mild specific infection, generally of shorter duration than pertussis, and it occurs in infective foci in the community in parallel with, or independently of, pertussis. The atypical clinical form, comprising cough without paroxysms, occurred in this study in a ratio of 8·6 to 1 of the typical paroxysmal form, an atypical/typical proportion 7 or 8 times as frequent as in pertussis. Symptomless carriers of *Haemophilus parapertussis* were discovered only in the milieu of the infective foci of parapertussis, and they were more frequent among those affected by, and those immunized against, pertussis than among those not previously affected by pertussis or immunized against it. It would appear that there is probably a common antigen between the 2 organisms, but that cross-immunity is not complete. This is shown also by the infectivity index among contacts; this averaged 35 for parapertussis among the child contacts in this study, but was 23·8 among those affected by pertussis, 25 among those actively immunized against pertussis, and 51 among those neither previously affected by pertussis nor immunized against it.

The material comprised 106 cases of parapertussis and 27 carriers, collected over a period of a year in 40 nurseries and kindergartens in Sofia.

H. Stanley Banks

LESNICAR, J. Zdravljenje pertusisa z vitaminom K in INH. [**The Treatment of Pertussis with Vitamin K and INH**] *Zdravstveni Vestnik.* Ljubljana. 1958, v. 27, Nos. 5/6, 231–4. [19 refs.] German summary.

On the basis of the hypothesis that the paroxysmal cough in pertussis is due to the presence of small haemorrhages in the respiratory mucosa the author has studied the effect of the treatment with vitamin K upon the course of the disease. About 100 patients aged 2 months to 6 years were given 10 mgm. of vitamin K subcutaneously for 7–10 days. In 85% the duration of the paroxysmal cough was reduced to 25 days in severe and 18–20 days in moderate forms of the disease. 30 patients were treated with a combination of vitamin K and isoniazid. *D. J. Bauer*

MCCARTHY, K., DOWNIE, A. W., & BRADLEY, W. H. **The Antibody Response in Man following Infection with Viruses of the Pox Group. II. Antibody Response following Vaccination.** *J. Hygiene.* 1958, Dec., v. 56, No. 4, 466–78, 8 figs. [28 refs.]

The authors examined post-vaccination sera for neutralizing and complement-fixing antibodies and anti-haemagglutinin. In the primary vaccination group neutralizing antibody was demonstrable from 13 days after vaccination. The highest titres of antibody were found in cases of generalized vaccinia. Significant levels of neutralizing antibody were found in the sera of people vaccinated only once 20 to 40 years previously. Complement-fixing antibody appeared at about the same time as neutralizing antibody, but a

number of cases were recorded in which a significant level of neutralizing antibody was not accompanied by an increase in complement-fixing antibody. Within 2 months of primary vaccination, titres of complement-fixing antibody had declined below the level of 1/5 which was the lowest tested. Antihaemagglutinin also appeared at the same time as neutralizing antibody. The general level declined rapidly thereafter, but a few sera had measurable antihaemagglutinin 20 years after primary vaccination.

After revaccination the neutralizing antibody response was usually brisk, but not always so. One of the figures shows the responses of 5 people after revaccination. Three show typical secondary responses, one a typical primary response and the fifth no response at all. The significant thing about this is that the fifth subject gave a "take" clinically indistinguishable from two of the subjects with secondary responses. Generally speaking neutralizing antibody levels after revaccination were higher than after primary vaccination and appeared sooner. Complement-fixing antibody and antihaemagglutinin behaved in much the same way as after primary vaccination. The authors think that the best *in vitro* assessment of immunity to smallpox is to be found in the level of neutralizing antibody rather than of complement-fixing antibody or anti-haemagglutinin.

The authors draw attention to the problem of early "takes" without vesiculation in revaccination. 28 subjects were tested for neutralizing antibody before and after revaccination, and their skin reactions were carefully noted. 15 of these had an early reaction without vesiculation: only 8 of them showed a subsequent increase in antibody. This is important, not only from the point of view of prophylaxis, but because prompt [and successful] revaccination of smallpox contacts may give greater protection than primary vaccination. [Antivaccinial gamma globulin given parenterally is probably the best protective treatment in the case of exposure of unvaccinated persons to smallpox.]

Colin Kaplan

DOWNIE, A. W. & MCCARTHY, K. **The Antibody Response in Man following Infection with Viruses of the Pox Group. III. Antibody Response in Smallpox.** *J. Hygiene.* 1958, Dec., v. 56, No. 4, 479–87, 3 figs. [17 refs.]

In cases of smallpox not previously vaccinated neutralizing antibody and antihaemagglutinin were present after the 6th day of illness in all cases and often by the 3rd or 4th day. Complement-fixing antibody was detectable after the 8th day.

In previously revaccinated cases of smallpox, antibody levels were higher, neutralizing antibody being present in all sera after the 3rd day and antihaemagglutinin after the 4th day. In 8 of 10 fatal cases antibody titres were low.

In *variola sine eruptione*, confirmation of the diagnosis may be made from a consideration of the patient's antibody levels.

The authors base their conclusions on the examination of 140 sera from 117 patients with smallpox.

[For Part I in this series, see this *Bulletin*, 1958, v. 33, 709.] *Colin Kaplan*

TADZER, I. S. **Hemorrhagic Disturbance in Rubella.** *Acta Med. Iugoslavica.* 1958, v. 12, No. 3, 233–45, 2 figs. [14 refs.]

In an extensive but mild outbreak of rubella 6 patients developed acute haemorrhagic systems. A low platelet count, increased capillary fragility and prolonged bleeding time were found in each case. In 20 non-haemorrhagic cases platelets were diminished and capillary fragility increased but to a lesser extent than in the haemorrhagic cases. Possible theoretical considerations are discussed. *A. B. Christie*

MURRAY, H. G. S. & MCALISTER, J. J. **Serological Investigation of University Students following the 1957 Influenza Epidemic in Northern Ireland.** *Ulster Med. J.* 1958, Nov. 1, v. 27, No. 2, 165–7.

Sera from 83 university students were tested by haemagglutination-inhibition (HI) against Asian influenza virus and by complement-fixation against influenza A and B soluble antigens, adenovirus, Sendai and mumps V and S antigens. HI tests against Asian influenza virus were positive in 55·4% of the sera. The proportion of students reporting symptoms regarded as clinical influenza during the preceding month was 98% among those with positive HI tests and 76% among the negative group. No serological evidence of infection with influenza B, Sendai or mumps virus was obtained and 2 possible adenovirus infections were detected.

H. G. Pereira

SCHWARZ, H. Beitrag zur Grippeepidemie 1957 in Ruhrgebiet. [**The Influenza Epidemic in the Ruhr in 1957**] *Arch. f. Hyg. u. Bakt.* 1959, Jan., v. 143, No. 1, 38–64, 10 figs. [Numerous refs.]

This is a very long paper in which the author first gives some account of influenza in past years in the Ruhr for comparison with the experience of Asian influenza in 1957 particularly in the Ruhr mining areas. A few cases occurred at the beginning of August after which the incidence increased greatly to a peak in September and by the end of October the epidemic had ceased. Separate sections of the paper deal with the introduction of the infection, the influence of meteorological conditions, incidence and crowding, duration of the epidemic, incidence by age and by sex, the influence of fatigue and of high temperatures at work and of exposure to "sub-toxic" gases during work. These aspects of the epidemic experience are elaborated and discussed with illustrative figures but few numerical data are given.

Among the conclusions it is stated that the dependence of the epidemic on bad weather was evident. In the mining industry the incidence was greater in the less populated than in the densely populated districts. The disease was most prevalent in young people. Heavy work appeared to lower the resistance of the miners to the infection. Miners working in a high temperature had a much lower sickness absence rate than other workers. Men engaged with coke ovens who are continually exposed to the fumes of sulphur dioxide were also less prone to suffer from influenza than other workers. *M. E. Delafield*

BLUMENFELD, H. L.; KILBOURNE, E. D.; LOURIA, D. B.; ROGERS, D. E.; ELLIS, J. T. **Studies on Influenza in the Pandemic of 1957–1958. I. An Epidemiologic, Clinical and Serologic Investigation of an Intra-hospital Epidemic, with a Note on Vaccination Efficacy** [BLUMENFELD, KILBOURNE, LOURIA & ROGERS]. *J. Clin Investigation.* 1959, Jan., v. 38, No. 1, Pt. 2, 199–212, 7 figs. [18 refs.] **II. Pulmonary Complications of Influenza** [LOURIA, BLUMENFELD, ELLIS, KILBOURNE & ROGERS]. *Ibid.*, 213–65, 30 figs. (4 coloured on 2 pls.) [43 refs.] **III. Isolation of Influenza A (Asian Strain) Viruses from Influenza Patients with Pulmonary Complications. Details of Virus Isolation and Characterization of Isolates, with Quantitative Comparison of Isolation Methods** [KILBOURNE]. *Ibid.*, 266–74, 1 fig. [16 refs.]

I. An outbreak of Asian influenza occurring among patients and staff of a hospital ward was studied by clinical and laboratory methods. Of 62 persons included in the study, 30 suffered clinical illness and 8 showed only serological signs of infection. A virus strain identified as Asian influenza was isolated from throat washings of 1 out of 5 patients. The symptoms observed were typical of influenza but it was noted that gastro-intestinal symptoms were more frequent in patients with underlying disease. Pulmonary complications were observed in 3 patients with rheumatic heart disease. Routine laboratory tests did not reveal consistent abnormalities, apart from occasional lymphocytopoenia. Antibody rises for Asian influenza virus were demonstrated in 31% (5 out of 16) of vaccinated and in 65% (24 out of 37) of unvaccinated subjects. Some correlation between magnitude of antibody rise and severity of illness was observed.

II. This is an extensive report on the pulmonary complications observed among patients with Asian influenza. 33 patients were studied and divided into 4 groups according to clinical and laboratory findings. The first group consisted of 3 patients with transient pulmonary signs without evidence of bacterial infection and recovering on symptomatic treatment alone. The second group included 15 patients with late bacterial pneumonia caused by pneumococcus (8 patients), staphylococcus (3 patients), influenza bacillus (1 patient) and mixed infection (3 patients). There was 1 fatal case in this group. The third group consisted of 9 patients with concomitant viral and bacterial infection with fatal outcome in 3 cases. Asian influenza A virus was isolated from the lungs of each of these 3 patients who died. Pneumococcal, staphylococcal and mixed bacterial infections were observed among these patients. The fourth group consisted of 6 patients with fulminating diffuse haemorrhagic pneumonia not associated with bacterial infection. The disease was fatal in all but 1 case and influenza virus was isolated from the lungs of 4 of 5 patients.

Chronic disease or pregnancy were common among the patients with pulmonary complications and 9 of the 11 deaths occurred among patients with underlying disease.

It is concluded that influenza virus may cause pneumonia in the absence of other pathogens and that underlying disease may play an important role in the pathogenesis of influenza virus pneumonia.

III. Different methods used for virus isolation from patients suffering from influenza with pulmonary complications were compared. Inoculation of pathological materials into the amniotic or allantoic cavities of fertile eggs gave positive results in comparable numbers. Treatment of eggs with cortisone did not increase their sensitivity to influenza virus. Attempts to isolate virus in monkey kidney cultures gave negative results. Combined mouse-egg passages of lung suspensions gave positive results only when the materials under test contained large amounts of virus. Virus concentration in the lungs from fatal cases was inversely correlated with length of illness.

No differences between virus strains isolated from fatal and non-fatal cases could be detected regarding mouse pathogenicity, haemagglutinating activity or morphology. *H. G. Pereira*

WATROUS, R. M., MCANDREW, M. J. & ROBBINS, Mary. **Asian Type A Influenza. Results of an Industrial Immunization Program.** *Indust. Med. & Surgery.* Miami. 1959, Jan., v. 28, No. 1, 12–14, 1 fig.

A monovalent Asian influenza vaccine was administered to 3,047 workers in a pharmaceutical industry. An extensive outbreak of respiratory disease believed to be caused by the Asian influenza virus started during the later part of the vaccination programme. The incidence of influenza occurring 2 or more weeks after vaccination was 7·8% which is compared with an incidence of 11·7% among 323 unvaccinated workers. 1·4% of vaccinated workers reported losing time from work as a result of reactions to the vaccine.

H. G. Pereira

SINCLAIRE, H. A., FLYNN, J., SAUNDERS, G. M., ERNEST, C. E. & ERICSON, O. A. **Inoculation against Asian Influenza.** *Indust. Med. & Surgery.* Miami. 1959, Jan., v. 28, No. 1, 15–19, 3 figs. [22 refs.]

The protective effect of a monovalent Asian influenza vaccine against cold or influenza-like illnesses was investigated by means of a questionnaire sent to 2,495 employees of a large international company. 1,746 (69·9%) of the questionnaires were returned, including 1,330 and 416 from vaccinated and unvaccinated employees respectively. Lost-time cases due to cold or influenza-like illnesses occurred in 31·3% of vaccinated and 38% of unvaccinated subjects. Lost-time was reported more frequently by women than by men and this difference is attributed to the fact that women are more "sickness prone" and less motivated to work when ill. The number of days lost due to cold or influenza-like illnesses was not affected by vaccination.

H. G. Pereira

VAN DER VEEN, J. & VAN DER PLOEG, G. Een epidemie van acute pharyngo-conjunctivitis. [**An Epidemic of Pharyngoconjunctival Fever**] *Nederl. Tijdschr. v. Geneesk.* 1958, Oct. 4, v. 102, No. 40, 1948–54, 3 figs. [17 refs.] English summary (8 lines).

In July 1957 an epidemic of acute pharyngo-conjunctivitis occurred in a town in Holland. A strain of adenovirus was isolated from the discharges or throat washings of 62 of 75 patients investigated (83%), and a 4-fold or greater rise in titre of complement-fixing antibody was observed in 22 patients from whom virus was isolated, and a positive result was also obtained with the sera of 31 of 32 other patients. 46 of the strains isolated were of type 3, 11 were type 4, 2 type 5, and types 2, 7 and 9 were encountered in single instances. Several hundred cases occurred in all. The onset was acute with fever but without rigors. Most patients complained of headache, often severe; follicular conjunctivitis developed, usually bilaterally, with photophobia, and also rhinitis and pharyngitis. The temperature returned to normal on the 5th to 9th day of illness, and most patients had recovered after 10 days. No complications were observed. Of 93 patients in whom the diagnosis had been confirmed by laboratory investigations 49 (63%) were children aged 8–14 years, and boys were affected twice as frequently as girls.

D. J. Bauer

CULVER, J. O., LENNETTE, E. H. & GREEN, Lucile. **Serologic Reactions in Adenovirus Disease. I. Delayed Complement-Fixing Antibody Response.** *J. Lab. & Clin. Med.* 1959, Feb., v. 53, No. 2, 241–6. [12 refs.]

"In young men with respiratory disease there was usually good correspondence between the isolation of an adenovirus and the appearance of an increase in complement-fixing antibody in about 2 to 3 weeks. In 9 of the 129 cases, an increase in complement-fixing antibody in this period of time was not demonstrable, but in 7 of these 9 instances a definitive increase in antibody titre could be found after 29 or more days. In 2 of the 9 cases, complement-fixing antibody failed to rise even at this late time.

"When the acute and late convalescent phase sera were assayed for neutralizing antibody, a rise in titer was detected in all 9 individuals in whom demonstrable complement-fixing antibody either failed to appear or was delayed in appearing. The neutralizing antibody response was often heterotypic, however, bearing no relationship to the virus serotype isolated from the individual."

GAISFORD, W. **Drug Treatment of Infants and Children suffering from Pneumonia.** *Brit. Med. J.* 1959, Jan. 24, 230–32.

For lobar pneumonia, "Stosstherapy" (treatment with a large single dose) is strongly recommended in children. The sulphonamides are effective in pneumococcal infections, and are the first choice in lobar pneumonia; the dosage is 1 gm. to 3 gm. daily according to the age of the child, and a combination of 2 or 3 sulphonamides is preferable. If the drug is vomited, penicillin should be given in a single large intramuscular dose of 1,000,000 units at age 2, to 2,000,000 units at age 5. The continued presence of slight fever and bronchial breathing is not an indication for further therapy.

For bronchopneumonia, stosstherapy is not enough, but any antibiotic should be given in maximum dosage for the shortest possible time. If for any reason, treatment is prolonged for a week or more, extra vitamin B is indicated, but not, as a rule, a prophylactic antimonilial drug.

For neonatal pneumonia treated at home, crystalline penicillin 250,000 units should be injected at once, followed by procaine penicillin 250,000 units daily; in hospital, where staphylococci are usually penicillin-resistant, streptomycin 0·125 gm. twice daily in addition is recommended where the infecting organism is the staphylococcus, and alone where it is *Escherichia coli*. In older infants, especially where *Haemophilus influenzae* or *H. pertussis* may be involved, chloramphenicol 125 to 250 mgm. every 4 to 6 hours is preferable, and should be given notwithstanding the very slight risk of aplastic anaemia.

In recurrent pneumonitis, cystic fibrosis of the pancreas or agammaglobulinaemia should be suspected. Antibiotics are given in the former according to the organisms present in the bronchial mucus. In virus infections there is no specific treatment, but on the assumption that a concomitant bacterial infection may be present, broad spectrum antibiotic (tetracycline group) should be given in dosage of 12–25 mgm./kgm. If there is no response within 2 or 3 days the infection is probably viral, and further bacterial cover may be by penicillin V orally. If spasm is a feature, relief may follow mepyramine maleate (Anthisan) in dosage of 5–25 mgm. with pethidine 5–10 mgm. according to the age of the infant. In overwhelming infections, hydrocortisone 5–10 mgm. twice daily by mouth for 3 or 4 days should be given in addition to an antibiotic.

H. Stanley Banks

FUSAROLI, A. Prime manifestazioni a carattere epidemico di meningite linfocitaria benigna nel Comune di Forlì. [**The First Epidemics of Benign Lymphocytic Meningitis in the Forlì Area**] *Riv. Italiana d'Igiene.* 1958, July–Aug., v. 18, Nos. 7/8, 304–13, 1 map & 1 graph. English summary (3 lines).

The first authenticated occurrences of benign lymphocytic meningitis in Italy were in the Marches and in Tuscany. A group of 70 cases occurred between 1945 and 1949 in Ancona and its surroundings. By the first half of 1955 the number of cases had reached 167. In the summer of that year there was an epidemic which produced another 652 cases. In another epidemic at Tirrenia, near Pisa, 74 children at a camp were affected. Coxsackie virus, group A, was isolated.

In the Forlì area cases appeared by the end of August 1955, first reports coming in from suburbs quite distant from each other. The epidemic had reached its climax by mid-September, decreased by the end of the month, and was at an end by mid-October.

It appears there were 412 cases reported, but investigations showed the real number to have been about 1,500. Incidence was greater in the outlying areas than in the centre, and children under 10 were more commonly affected. There were few multiple cases in the same family. Clinically a sharp feverish onset was followed by myalgia, headache and pharyngeal pain, sometimes accompanying deglutition. Digestive disturbances were frequent. This condition passed off in 3 to 4 days except in the cases where meningism appeared and in the cases, which were rare in Forlì, with definite meningitis. The cerebrospinal fluid showed moderate increase of albumin and globulin. Cells were scanty, consisting of leucocytes including some polymorphonuclears. Only in a few patients were there relapses. Coxsackie virus group A was isolated.

The epidemic in Forlì appeared to derive from that in Ancona and its surroundings. This new focus of Coxsackie disease appears to have cleared up since by 2 years later only about 10 more cases had appeared in Forlì. *E. Agius*

MELÉN, B., WRANGE, G. & OLIN, G. **Antibodies to Poliomyelitis in School Children in Stockholm.** *Arch. f.d. gesamte Virusforschung.* 1958, v. 8, No. 4, 437–45, 1 fig. [18 refs.]

In March 1955 in Stockholm, and October 1956 in Solna, blood samples were drawn from children in third grade (usually 7–9 years old) before poliovaccination. Sera from all the Solna children (602) accepting vaccination and from a random sample (862) of the Stockholm children were examined undiluted for poliovirus neutralizing antibodies. It was found that there was little difference between the 2 communities except that the Solna children had more Type 3 antibodies. The sera from Solna children were drawn 1½ years later than those from Stockholm and during this period Type 3 virus was the most prevalent type isolated from poliomyelitis cases in Sweden. The level of immunity was similar in both sexes, and in all age-groups and in schoolchildren drawn from different socio-economic conditions. There were only slight tendencies to a higher incidence of antibodies in the older children and in those from poorer districts.

About 30% of the children lacked antibodies to all 3 types of virus and 8% in Stockholm and 17% in Solna had them to all 3 types. The antibodies to the 3 types did not appear to occur independently of each other. There was a higher proportion of children with no antibodies or all 3 types than would be expected from the overall frequency of the different types of antibody. Even excluding this factor, there were in Stockholm more children with Type 1 and 2 antibody than would be expected if the viruses spread independently. It was found that a higher proportion of children had a low titre (only 1 of 2 cultures protected with undiluted serum) to Type 2 than to the other types. It is thought that this might mean that Type 2 antibodies are heterotypic responses to Type 1 infection. Alternatively an individual who is living under conditions likely to expose him to one type of poliovirus is probably more likely to acquire infections to other types, than an individual living in a more sheltered environment.

From the incidence of antibodies and the incidence of paralytic poliomyelitis it was estimated that the frequency of a paralytic outcome of primary poliovirus infection was 5 per 1,000. *A. J. Beale*

HASEEB, M. A. **Poliomyelitis in the Sudan.** *J. Trop. Med. & Hyg.* 1959, Feb., v. 62, No. 2, 45–6.

"1. Forty-six sera from children in the urban city of Khartoum and forty-eight sera from children in the rural district of Kassala were tested for poliovirus antibodies.

"2. All sera neutralized one, two, or all three types of poliovirus."

GERLOFF, R. K., LARSON, C. L. & GLESNE, Lillian R. B. **Naturally Occurring Poliomyelitis Antibody in Hamilton, Montana.** *Pub. Health Rep.* Wash. 1959, Feb., v. 74, No. 2, 175–80, 1 chart. [11 refs.]

"Incidence of poliomyelitis antibody resulting from natural infection in a relatively isolated rural community of western Montana was determined by tests of 1,034 serums collected from residents, mostly children, in and near the town of Hamilton. Neutralizing antibody to all three types of poliovirus was present, but in nearly all age groups type 1 antibody was the most prevalent and type 3 the least prevalent. Incidence of antibody generally increased with increasing age of the population, but spread of poliovirus has been much slower in this community than in densely populated areas. Only 5 percent of the high school pupils, aged 14–17, had been infected by all three types of virus. High antibody titers occurred more frequently in children than in adults. Multiple children in individual families were, in most instances, either all immune or all non-immune to a particular type of virus, a fact which portrays the importance of household contact in spread of poliovirus through a community."

THIEFFRY, S., MARTIN, Charlotte & ARTHUIS, M. Sur 170 cas de poliomyélite respiratoire traités à l'hôpital des Enfants-Malades de 1950 à 1957. [**On 170 Cases of Respiratory Poliomyelitis Treated at the Sick Children's Hospital, Paris, from 1950 to 1957**] *Bull. Acad. Nat. Méd.* 1958, v. 142, Nos. 33/34, 933–40.

The authors describe their experience with 170 cases of respiratory poliomyelitis occurring between 1950 and 1957. Of the total, 57 patients had respiratory embarrassment due to paralysis of swallowing and only 2 died. The other 113 patients had paralysis of the respiratory muscles: 81 of these were "dry" cases and of these 18 died: 32 were "wet" cases and 23 died. In 1955, the authors began to practise tracheotomy and positive pressure ventilation for these wet cases. Before 1955, 18 out of 20 wet cases died: after 1955, 5 out of 12 died. *A. B. Christie*

REMENCHIK, A. P., DYNIECWICZ, Josephine M. & SCHOENBERGER, J. A. **Changes in Body Composition during the Course of Acute Anterior Poliomyelitis.** *J. Lab. & Clin. Med.* 1959, Feb., v. 53, No. 2, 195–215, 3 figs. [84 refs.]

J. HYG., EPIDEMIOL., MICROBIOL. & IMMUNOL. Prague. 1958, v. 2, No. 4, 415–83, numerous figs. [Numerous refs.] **Papers on Poliomyelitis and Vaccination.**

In 8 papers a comprehensive account is given of the poliovaccination programme carried out in Czechoslovakia in 1957 including the epidemiological background and an account of the virus diagnostic procedures. The papers are well worth reading in full. V. ŠKOVRÁNEK *et al.* (pp. 415–22) review the rising incidence of poliomyelitis in Czechoslovakia since the first epidemic in 1939, which led to the decision to use poliovaccine in 1957. Because of shortage of vaccine it was decided to use the intradermal technique with 0·1 ml. of vaccine for the first dose and 0·15 ml. for the second dose according to the method of VON MAGNUS *et al.* [this *Bulletin*, 1956, v. 31, 499].

3 papers describe serological surveys for poliomyelitis antibodies. In the first K. ŽÁCEK *et al.* (pp. 423–37) describe an extensive survey in 3 areas of Czechoslovakia—Prague, Jihlava and Ústí. In Prague and Jihlava 50% of the children had antibodies to the individual types of poliovirus by the age-group 6–9 years, but the incidence of clinical poliomyelitis is about 3 times greater in Prague. In Ústí, on the other hand, antibodies develop earlier, 50% of the children having them by the age of 3–5 years. Children living in agricultural areas developed antibodies to poliovirus more slowly than children living in industrial areas but this later age of acquisition of antibodies was not correlated with an increased incidence of poliomyelitis. E. ADAM *et al.* (pp. 438–42) attempted to find children lacking antibodies to all 3 types of poliovirus to use for the assessment of the serological response to intradermal or subcutaneous inoculation of poliovaccine. They found that children in orphanages acquired antibodies at a much earlier age than children in the normal population. They also found that the incidence of antibodies to all 3 types of poliovirus increased with the length of stay of the children in the homes. Despite the high incidence of poliovirus antibodies among these children there were no records of outbreaks of clinical poliomyelitis. J. PESEK (pp. 443–7) studied the incidence of antibodies to poliovirus in Slovakia and he found that 50% of the children have antibodies against Type 2 and Type 3 virus by the age of 3 years and to Type 1 between 3 and 5 years. Pešek employed the *p*H inhibition or colour test method for the detection of poliovirus antibodies and found that this method was rather more sensitive at low levels of antibody than the conventional method with roller tube cultures.

K. ŽÁCEK *et al.* (pp. 448–56) discussed the diagnostic methods used. They found monkey kidney cells from *Macaca irus* and *M. mulatta* monkeys were very efficient for the isolation of viruses from cases of paralytic poliomyelitis. They found they had an isolation rate of 80% from paralytic cases and 18% from patients with isolated seventh nerve palsy and 9·5% from patients with meningitis. They stress the value of the complement-fixation test for the rapid diagnosis of poliomyelitis by the method devised by BLACK and MELNICK (*Yale J. Biol. & Med.* 1954, v. 26, 385) provided the antigens are treated with fluoro-carbon to remove the anti-complementary effects as described by HUMMELER and HAMPARIAN [this BULLETIN, 1957, v. 32, 1205]. V. VONKA and ŽÁCEK (pp. 457–68) describe the isolation of other human enteric viruses besides poliovirus during the virological control of the vaccine programme. In all, 994 sick children were examined and 116 enteric viruses other than poliovirus were isolated. The isolation rate was 15% in patients suffering from meningitis. The strains that have been typed so far have proved to be ECHO 9, 66, Coxsackie A9, 19, Coxsackie B2, 5 and B1, 3.

An attempt was made to assess the efficacy of the poliovaccine programme (V. ŠKOVRÁNEK *et al.*, pp. 469–77). The vaccine was administered to children 1–7 years old and in a few cases to older children. The vaccination programme started in May and continued during June of 1957. Nearly 90% of the children aged 1–7 eligible for vaccination were, in fact, vaccinated. The method of evaluation of the results was similar to that employed in the Francis trial, the study being along the lines of the observed areas in the American trial. No attempts were made to show that the children accepting vaccination and those refusing it were similar. There was no evidence that the vaccine induced any cases of poliomyelitis. Paralytic poliomyelitis was about 3 times as prevalent in non-vaccinated children as in vaccinated children in the age-group 1–7 years. In the final paper J. PROCHÁZKA *et al.* (pp. 478–83) describe the clinical criteria used for the diagnosis of paralytic poliomyelitis. They also describe the features of the illness in 143 vaccinated and 67 non-vaccinated children. They found that there were no differences in the clinical features of poliomyelitis in the vaccinated or unvaccinated children. *A. J. Beale*

VIVELL, O. & LIPS, G. Komplementbindungsreaktionen mit dem ECHO-Virus Typ 9 (Coxsackie-Virus Typ A 23). [**Complement-fixation Tests with ECHO-9 (Coxsackie Type A23) Virus**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 2, 131–42, 1 fig. [58 refs.]

Satisfactory complement-fixing antigens have been prepared from infant mice infected with 2 mouse-adapted strains of ECHO-9 virus. The animals were killed when paralysis was well advanced, and the skeletal musculature was dissected away from the carcases, frozen, ground with sand and taken up in 20 volumes of acetone. The sediment was recovered by centrifugation, treated again with 20 volumes of acetone, recovered and washed similarly with acetone-ether and twice with ether. The residue was dried in a desiccator and then dissolved in 2 volumes of saline; after standing in the cold for 24 hours and ultracentrifugation for 1 hour it was used as antigen in

complement-fixation tests with mouse immune serum. The muscle antigen gave good results, but satisfactory antigens could not be obtained from infant mouse brain or tissue culture fluid. In complement-fixation tests with muscle antigen positive results were obtained with the sera of 60 of 89 patients with abacterial meningitis and with 66 of 191 control sera.

D. J. Bauer

DOWLING, M. A. C. & WEBB, H. E. **A Preliminary Report on Encephalitic Type of Illnesses in Singapore.** *J. Roy. Army Med. Corps.* 1959, Jan., v. 105, No. 1, 28–37, 2 figs.

This is a study of the case-histories of 333 patients admitted to the general and military hospitals in Singapore between 1954 and 1956 with symptoms of central nervous system disease other than of the lower motor neurones. 88 patients were military and 245 Asian civilians, with 15 and 77 deaths respectively. The majority of the civilian patients were Chinese aged 0–10 years while the Europeans were mainly 20–40 years of age. 74% of the cases among Europeans occurred within 2 years of arrival in the Colony. Case fatality was highest (34%) in Asian children aged under 10.

The symptoms comprised severe headache, vomiting, fever which was often very high and often suffusion of the upper trunk, face and conjunctivae. Mental changes were common. There was no lymphadenopathy, splenomegaly, rash or eschar. Some patients had stiffness of the neck but no further signs from the central nervous system. In more severe cases convulsions often heralded various nervous complications which might be followed by coma and death. Coma in adults had a bad prognosis. Nervous complications included cranial nerve lesions, tremors, ataxia, hemiplegia. Circulatory failure apparently of central origin supervened in some patients.

In Gurkha children aged 6 to 18 months there was a common syndrome of mild respiratory symptoms followed by vasomotor collapse, coma and often death within a few hours. Lung signs were detected only after onset of coma and abnormalities of the pupils were the only pointers to the central nervous system. The cerebrospinal fluid contained excess cells and protein but normal sugar and chlorides. At post-mortem signs of pneumonitis and encephalitis were found.

The geographical distribution of cases appeared to be focal in both urban and rural localities. This suggested a relationship to the trombiculid mite *Euschöngastia indica* and dieldrin fogging was therefore carried out in the military areas. A dose of 4 oz. per acre lasted less than a month as judged by mite indices. 10 oz. per acre repeated after 2 months gave control for 5–6 months and no further cases occurred in treated areas but continued elsewhere.

Investigations are being made into the aetiology of these illnesses but no information is yet available. The authors believe that arborviruses are responsible. [It seems unlikely that all the cases grouped here are of similar aetiology but that this may be highly complex.]

C. E. Gordon Smith

LONGSHORE, W. A., Jr. El problema de la encefalitis en California. [**The Encephalitis Problem in California**] *Bol. Oficina Sanitaria Panamericana.* 1959, Jan., v. 46, No. 1, 39–47, 19 refs. English summary.

IGNJATOVIC, B. **Typhoid Fever in Kragujevac during a Period of 30 Years (1926–1956).** *Bull. Inst. Hyg.* Belgrade. 1957, v. 6, Nos. 3/4, 13–20, 2 figs. [In Serbian.] English summary.

Data are presented on the incidence of typhoid between 1926 and 1956 in Kragujevac, Serbia, a town with a population which has increased from 22,000 to 45,000 during the period under review. Between 1926 and 1938 the annual number of cases ranged from 6 to 54, representing a maximum incidence of 15·88 per 10,000. In 1938 a new water supply was installed, and the annual number of cases fell to 2–17, with a maximum incidence of 5·31 per 10,000. There were 17 fatal cases between 1929 and 1938, 7 between 1939 and 1948 and 1 between 1949 and 1956; the mortality per 100,000 in the 3 periods was 5·23, 2·22 and 0·31 respectively. The data suggest that typhoid in Kragujevac was originally a water-borne infection and has been largely eliminated by improving the water supply.

D. J. Bauer

GAVRILĂ, I., COMES, L., MURESAN, T., BUCIU, M., IGNA, M., CUCU, A. & SERBAN, I. Comportarea titrului aglutininelor anti-H si anti-O în febra tifoidă tratată cu cloramfenicol. [**The Behaviour of the Titre of Anti-H and Anti-O Agglutinins in Typhoid treated with Chloramphenicol**] *Microbiol., Parazitol. si Epidemiol.* Bucharest. 1958, Jan.–Feb., v. 3, No. 1, 55–64. English summary (8 lines).

An investigation has been made of the course of development of anti-H and anti-O agglutinins in 396 patients suffering from typhoid, 212 of whom received specific treatment with chloramphenicol which was usually begun between the 4th and 12th days of illness. In titrations of anti-H agglutinin a rise in titre after chloramphenicol treatment was found in 22 of 33 patients with an initial titre of 80 and in 21 of 42, 15 of 45, 16 of 26 and 6 of 30 with initial titres of 160, 320, 640 and 1,280 respectively. There was no essential difference in the formation of anti-H agglutinin in the treated as compared with the control group, and the same conclusion could be drawn from the results of titrations of anti-O agglutinin in the 2 groups. *D. J. Bauer*

JELLARD, C. H., JOLLY, H. & BROWN, R. N. **An Outbreak of *S. bovis-morbificans* Infection in a Children's Ward.** *Lancet.* 1959, Feb. 21, 390–92.

A few outbreaks of *Salmonella bovis-morbificans* infection have been recorded which were either of explosive food-poisoning type or were marked by gradual case-to-case spread [this *Bulletin*, 1949, v. 24, 697, 889]. The outbreak described in this paper began in a girl of 6 months who had had diarrhoea with blood and mucus for a week before admission to a children's ward on a provisional diagnosis of intussusception. No surgical cause was, however, found for her symptoms but *Salm. bovis-morbificans* was isolated from the faeces. The

patient probably acquired the infection from her brother who was found to be a symptomless excreter. Examination of the parents was negative. The brother sometimes travelled in his father's lorry used for transporting cattle and from the floor of this lorry, even after it had been cleaned with cresol and soap solution, the organism was also isolated.

No further cases of infection by the organism were discovered in the children's ward in spite of regular faecal examinations until 2½ weeks after the original patient had been admitted, when a baby who had developed mild diarrhoea after admission was found to be infected. Ultimately in the course of 2½ months from the admission of the original patient a total of 9 children and 4 nurses were discovered to be infected but of these only 3 of the children had any clinical manifestations.

There is a description of the careful investigations which were made to discover the mode of spread of the infection in the ward and the conclusion was that it "may have been spread during the mangling of napkins, which were assumed to have been sterilized by immersion in a disinfectant". Nurses carried out the mangling after the napkins had been kept in 40% benzalkonium chloride for 12 hours, a procedure which tests suggested was inadequate for disinfection.

M. E. Delafield

ALTSHULER, L. N. & HERNANDEZ, D. J. **An Epidemiological Study of an Outbreak of Water-Borne Dysentery.** *Amer. J. Pub. Health.* 1959, Jan., v. 49, No. 1, 82–93, 7 figs.

A sharp outbreak of diarrhoea occurred among U.S. troops and their dependants stationed in a particular locality in Germany. The disease was not severe and does not appear to have been a true dysentery; in spite of very frequent stools there was no record of the presence of blood and mucus, only watery diarrhoea. The outbreak lasted for about a week with a peak incidence on the 5th day and involved more than 1,000 persons in all. There is no detailed account of the clinical condition and there was no bacteriological investigation of any of the patients at the time so that the agent responsible for the outbreak was never identified. Rectal swabs taken later were negative for enteric pathogens. The pattern of the outbreak suggested, however, that the agent was food- or water-borne and epidemiological studies eventually showed that the water supply was heavily polluted with faecal bacteria. The source of the water was a well fed from several springs and there was a series of inspection shafts along the conducting system. In the vicinity of the last inspection shaft trenching-work had resulted in heavily polluted water from a nearby stream being carried to the ground round the entrance to the shaft. This ground was contaminated with the water from the stream, seepage was taking place and furthermore the polluted water was actually dripping into the water supply of the population involved.

The outbreak was effectively controlled, but the investigation revealed a number of weaknesses in water-engineering procedures and an unsatisfactory chlorinating system which had actually broken down just before the outbreak occurred. It is surprising to find no evidence of bacteriological examination of the water supply until after the outbreak had started. From the account given it would seem that although the outbreak was more or less "explosive" the pollution of the drinking water was built up more slowly; regular "presumptive coli counts" should have given adequate warning in time to avert the outbreak.

H. J. Bensted

BECSEI, D. A dizentéria szezonalitásáról. [**Seasonal Factors in Dysentery**] *Népegészségügy.* Budapest. 1958, May–June, v. 39, Nos. 5/6, 132–40, 7 charts. [16 refs.]

The importance of flies in the transmission of dysentery has been studied by comparing the seasonal incidence of dysentery between 1950 and 1956 in the inner suburbs of Budapest, which have a sewerage system, and the outer suburbs, in which sanitary conditions are primitive. No differences were observed between the 2 areas, either in the percentage incidence or in the form of the seasonal curve, which in both cases showed a peak in August, and it is concluded that transmission by flies is not of importance in the spread of dysentery infection. The peak of incidence of dysentery in the summer months is ascribed to the greater prevalence of gastro-intestinal disorders at this time, many of which may be mild cases of dysentery, which increase the dissemination of *Shigella* among the population.

D. J. Bauer

HUGH-JONES, K. & ROSS, G. I. M. **Epidemics of Gastro-Enteritis associated with *Esch. coli* O119 Infection.** *Arch. Dis. in Childhood.* 1958, Dec., v. 33, No. 172, 543–51, 5 figs. [15 refs.]

This paper describes 3 outbreaks of gastro-enteritis occurring in a baby ward between September 1954 and February 1956; each outbreak was associated with *Escherichia coli* O119. During the epidemics, out of 116 infants at risk, 41 were found to be infected, 20 of whom had gastro-enteritis and 7 had mild symptoms: there were 3 deaths, but 2 of these infants had congenital abnormalities. During the 2 interim periods between epidemics, various improvements were instituted in equipments, staffing arrangements and technique —these, together with terramycin therapy, reduced cross-infection, but it was obvious that the high infectivity rate and short incubation period could overcome these improvements and still produce epidemics. All the strains of *E. coli* O119 isolated had identical biochemical reactions and the same flagellar antigen (H6), and all were insensitive to sulphonamide; the authors stress that sensitivity tests should be carried out on all pathogenic *E. coli* strains isolated, as there is considerable individual variation.

John S. Stevenson

TUBERCULOSIS

GRIEP, W. A. Besmettingsleeftijd en ziektekansen bij tuberculose. [**Age of Infection and Incidence of Disease in Tuberculosis**] *Nederl. Tijdschr. v. Geneesk.* 1958, Aug. 16, v. 102, No. 33, 1592–5. English summary.

An investigation has been made of the subsequent history of 377 children and adolescents aged up to 18 years who experienced primary tuberculous infection between 1932 and 1942, with the object of determining the relation between age of contracting primary infection and subsequent liability to develop pulmonary tuberculosis. During the period of observation, which was continued up to 1957, 35 developed pulmonary tuberculosis (9·3%) compared with 69 of 1,064 (6·5%) of a comparable control group of persons who responded to exposure only by developing a positive tuberculin reaction. The numbers of cases according to age-groups were as follows: 0–5 years, 9 of 149 (6%); 6–11 years, 6 of 119 (5%), and 12–18 years, 20 of 109 (18·3%). A similar preponderance in the 12–18-year age-group was also seen in the control group, and also when the effect of the reduced period of observation of the younger age-groups was eliminated.

D. J. Bauer

CAMPHYN, R. & FREBUTTE, P. Méningites, pleurésies, polysérites et polyadénites tuberculeuses chez le noir. [**Tuberculous Meningitis, Pleurisy, Polyserositis, and Polyadenitis in the Negro**] *Ann. Soc. Belge de Méd. Trop.* 1958, Aug. 31, v. 38, No. 4, 605–38, 1 fig.

Tuberculous meningitis has been considered by many to be rare in Negroes but the authors have not found it so. In the period 1952–6 39 of 2,491 tuberculous patients admitted to their hospital in the Belgian Congo had tuberculous meningitis (1·2%), and to this number must be added the unknown number of children with the disease who were treated in children's hospitals and of patients who were not admitted to any hospital.

27 of the 39 patients (70%) were aged 0–9 years. 14 of these were under 4 years, mostly under 1.

23 (59%) died, 16 in the first 15 days after admission. Unfavourable factors were the duration of illness and the association of meningitis with other tuberculous lesions. Extra-pulmonary disease was the commonest addition in children but in adults the meningitis was most commonly combined with miliary disease, tuberculous bronchopneumonia or ulcero-caseous pulmonary tuberculosis. Many of the patients were also debilitated by ankylostomiasis and malnutrition (*e.g.* kwashiorkor).

The microscopic and chemical findings in the cerebrospinal fluid are described in detail. The only certain prognostic factors were the presence of tubercle bacilli on direct examination (bad) and of a polynuclear cell reaction (good because of denoting an early stage of the disease).

Up to 1953 the patients were given PAS and intramuscular and intrathecal streptomycin; after 1953 the following treatment was given:

(1) Streptomycin intramuscularly, 1–1·5 gm. daily for an adult in the early weeks.

(2) PAS, 15 gm. daily intravenously or orally or subcutaneously with hyaluronidase.

(3) Isoniazid orally, 20–40 mgm./kgm.

Corticotrophin was given in some cases, and Largactil [chlorpromazine] was used to control vomiting or convulsions. Treatment was continued in hospital for 6–8 months and for several months longer after discharge. Only 2 patients relapsed, both of whom had absconded from hospital before the sixth month.

Tuberculous pleural effusion was seen in 292 patients (10·8%), none of whom was under the age of 1 year. The greatest incidence was at 20 years with a decline thereafter. It was a manifestation of early post-primary disease. Both sides were affected in 23·5%, and other tuberculous foci were present in 57%. The death-rate was 10·8% (5·5% when pleurisy alone was present, 7·6% when other non-serous lesions were present and 43% when other serositis was present). Corticotrophin was found to be of great benefit in treatment.

Tuberculous polyserositis occurred in 37 patients in various combinations of site. The total death-rate was 46%; when there were 2 sites it was 40·6% and when 3 were combined it was 80%. The presence of meningitis was especially unfavourable. The youngest patient was aged 4 years, and the greatest incidence was at 5–10 and 20–30 years. Only 5 patients with polyserositis had associated tertiary tuberculosis; the rest were in the early post-primary stage.

Enlargement of the liver was found in 8 patients. It was probably due to tuberculosis but in the absence of biopsy other causes could not be ruled out. Rapid response to specific treatment in some cases was taken as evidence of the condition being tuberculous.

Tuberculous polyadenitis (excluding tracheo-bronchial adenopathy) was seen in 73 patients (2·9%). Diagnosis did not present any particular difficulty but the possibility of other causes of gland enlargement than tuberculosis must not be forgotten. Most of the patients were under 30 years; the greatest incidence was between 5 and 9 and 20 and 24 years. The youngest patient was aged 3 years. The death rate was 16·4% but death was rarely due to polyadenitis itself. The glands sometimes reached an immense size so that disturbance of the lymph circulation led to elephantiasis of scrotum or leg.

H. G. Calwell

DEENY, J. **The National Tuberculosis Survey of Ceylon.** *Irish J. Med. Sci.* 1959, Feb., 6th Ser., No. 398, 49–72.

The main object of this survey was to determine the prevalence of tuberculosis in Ceylon (population almost 9,000,000), and to provide reliable epidemiological information on which to base control and preventive measures. Action was necessary because for some years past tuberculosis has been officially recognized as the major disease affecting the country.

The survey was begun and completed in 1956 under the guidance of a WHO consultant and it followed closely the pattern of the tuberculosis survey of the

Republic of Ireland in 1950–3 [this *Bulletin*, 1955, v. 30, 210]. A random sample of persons was chosen from tea estate workers and rural, semi-rural and urban dwellers. 16,225 persons were included, and a 96% response was secured. The age-sex distribution of the sample was representative of the general population.

166 persons showed radiological evidence of active pulmonary tuberculosis, from which it was estimated that the incidence of active disease throughout the whole country is 0·8–1·2%. The estimated incidence of healed disease was 0·4–0·7%. The lowest incidence of active disease was between the ages of 15 and 34 with a steep rise after 45. It is possible that a real difference between the sexes exists, but it would require a larger sample and more elaborate analysis to demonstrate it. The same qualification applies to the finding that there was a higher rate of active disease in estate and urban sectors than in rural areas and higher rates for healed disease in the urban sector.

It was estimated that the total number of persons with active disease in the whole population must be about 63,000, of whom about 17% are males aged 45–64 years. Among the 1·3 million people aged 25–34 years one might expect to find 9,000 with active tuberculosis and in the 1·4 million aged 45 and over one might expect to find 24,000.

From the clinical findings in the sample it was estimated that in the total population there are 38,000 persons with primary lesions, 31,000 with infiltrative and 22,000 with mixed-type tuberculosis. Lung cancer was not discovered in any person in the sample.

At least 1 bacteriological examination was made in 217 (87·5%) of the 248 persons recalled for further examination by large film, and tubercle bacilli were found in 26; the overall positivity rate was 15·6% of those with unhealed and 5·3% of those with "healed" disease.

The survey showed that the problem of controlling tuberculosis in Ceylon lies in the rural areas and that the reservoir of infection is mainly in the older groups. Housing and nutrition will have to be attended to in addition to the application of ordinary means of control such as detection, treatment and contact examination and vaccination. *H. G. Calwell*

BUTZENGEIGER, K. H. & GEISSEN, W. Über die Tuberkulin-Empfindlichkeit des gesunden und des tuberkulose-kranken Menschen und ihre klinische Bedeutung. [**Tuberculin Sensitivity of Healthy and of Tuberculous Persons**] *Deut. med. Woch.* 1959, Jan. 23, v. 84, No. 4, 142–7, 175. [34 refs.]

The tuberculin test has been neglected as a diagnostic measure because at one time practically all adults were reactors. This is no longer so and the authors have therefore thought it important to study tuberculin sensitivity in both tuberculous and non-tuberculous persons aged 15 years and over.

The Mantoux test was used with purified tuberculin ("GT Hoechst"). Non-tuberculous persons were given dilutions of 1 : 100 million to 1 : 100 thousand initially rising by multiples of 10 to undiluted tuberculin if there was no reaction to a smaller dose. The initial dilution used for tuberculous persons was 1 : 1,000 million or even higher. Reactions were read at 48–72 hours and induration measured. A subsidiary investigation was made which concerned the value of a tuberculin ointment "Hamburger forte" in percutaneous testing.

The non-tuberculous group consisted of 507 hospital patients (230 males and 277 females):

	Males Reactor rate %	Females Reactor rate %
Ointment	58·6	46·9
Mantoux 1 TU	16·9	32·8
10 TU	18·2	12·6
100 TU	5·2	4·3
1,000 TU	1 person	3 persons (1%)
1,000 TU	1 person did not react	6 persons did not react (2·1 %)

The lower reactor rate in females to the percutaneous test suggested that the skin of the males was more easily penetrated by the ointment. There was little difference in the reactor rates in the various age-groups.

300 persons in the group showed small calcified pulmonary foci, 77 large calcified foci and in 97 there was no radiological evidence of calcification. No difference in sensitivity was found between these 3 subgroups.

The influence of intercurrent disease and of repeated testing on the degree of sensitivity was not found to be significant.

The group of patients with active tuberculosis numbered 113. Sensitivity was studied in relation to the type of disease present and to treatment (chemotherapy). Full details are given in 2 tables. It was found that 52 patients had high sensitivity (reaction to 1 : 100,000 or higher dilution) of whom 40 had exudative or exudative-productive disease. Of 75 patients with cavitation 41 had high sensitivity and 34 lower sensitivity (reaction to 1 : 10,000 or lower dilution). The highest degree of sensitivity was found in 3 patients with recent exudative-cavernous disease, 1 with recent reactivation and 1 with exudative-productive silico-tuberculosis of several years duration. 2 patients reacted only to 1 : 100 dilution, 1 of whom had almost healed pulmonary and the other healed miliary and spinal tuberculosis.

52 of 90 patients who had not yet received chemotherapy were found to have the higher degree of tuberculin sensitivity whereas all of 23 patients already treated only reacted to dilutions of 1 : 10,000 or less.

In 56 of the 113 patients with active tuberculosis there was no change in the degree of sensitivity, in 47 there was a rise, in 4 a fall, in 4 a fall followed by a rise and in 2 a rise followed by a fall.

The results did not show a uniform pattern and no reliable conclusions could be reached about the relationship between tuberculin sensitivity and type of disease, resistance or prognosis. *H. G. Calwell*

ARAKAWA, T., OOTA, M. & SATO, Y. **The Erythrocytes sensitized with Tuberculin-Polysaccharide in the Circulating Blood of Children:—Their Diagnostic Application for Tuberculosis in Infancy and Childhood (Studies on Tuberculosis in Infancy and Childhood.** 3rd Report). *Tohoku J. Exper. Med.* 1958, Aug. 25, v. 68, No. 2, 105–13, 3 figs.

Having demonstrated in rabbits that in the earlier stages of experimental tuberculosis the red cells are sensitized with tuberculo-polysaccharide (*Tohoku J. Exper. Med.*, 1958, v. 68, 93), the authors now report a similar finding in children.

They examined the blood of 278 tuberculin-negative children, with histories of anorexia, vomiting, diarrhoea etc. Of 121 of these children aged 0–3 years 47 were positive for these cells, of 80 aged 3–7 years 27 were positive, and of 77 children aged 7–13 years 15 were also positive. The percentages with radiological evidence of tuberculosis were 44·6% aged 0–3, 66·6% aged 3–7 and 80% of the oldest group. None of the patients had circulating antibodies for the tuberculo-polysaccharides although 36% of the youngest group, 70% of the middle group and 80% of the oldest group had antibodies detectable with tuberculo-proteins assumed, in view of the absence of antibodies to the tuberculo-polysaccharides, to be derived from some other antigen.

The authors conclude that the detection of these sensitized cells may be a valuable indication of early tuberculosis in children under 7 years.

S. R. M. Bushby

ROYAL NETHERLANDS TUBERCULOSIS ASS. **Pulmonary Tuberculosis and Asthmatic Bronchitis. Coincidence and Mutual Relationship.** (ORIE, N. G. M.). *Proc. Tuberculosis Res. Counc.* 1957, No. 44, 5–33, 8 figs. [63 refs.]

Using Pasteur's remark "*Le grain n'est rien, c'est le terrain qui est tout*", the author discusses the relationship between asthmatic bronchitis and pulmonary tuberculosis, and parallel hormonal influences in tuberculosis, asthma and bronchitis. The argument is complicated by the statement that bacterial bronchitis and emphysema are allergic affections.

It is stated that at the Davos Sanatorium relapses are more frequent in patients whose pulmonary tuberculosis is complicated by asthma, and it is suggested that a basic factor underlies the unfavourable reaction to tuberculosis and the existence of the asthma.

Tables are given showing the frequency of asthma as detailed by various authors, and the frequency of asthma and asthmatic bronchitis in tuberculous patients, and it is concluded that although the figures vary very widely these occur more frequently in pulmonary tuberculosis than in the normal population. The author also quotes TEN HAVE'S figures that Boeck's sarcoidosis also appears more frequently in patients with a previous asthmatic history than in the normal population.

The remainder of the paper deals with a suggestion that exacerbation of tuberculosis may be connected with increased activity of the pituitary-adrenal system. Graphs are given to show that the excretion of 17-ketosteroids and 21-hydroxycorticoids are increased in age-groups in which the morbidity and mortality from tuberculosis unmodified by chemotherapy are higher. LURIE'S work on the increased susceptibility to tuberculosis of rabbits treated with cortisone is quoted, and connected with the effect of steroids on asthma. The author asks: "what is the frequency of coincidence of asthma and asthmatic bronchitis and pulmonary tuberculosis in different age-groups? Asthma and asthmatic bronchitis should be separated in the answer".

This very stimulating paper is so discursive that it is very difficult to abstract, especially as it propounds and discusses problems rather than tries to solve them. It will repay reading.

F. H. Young

TREIP, C. & MEYERS, D. **Fatal Tuberculosis in a General Hospital. A Diagnostic Problem.** *Lancet.* 1959, Jan. 24, 164–7, 4 figs.

This is a study of 128 necropsies performed at the Central Middlesex Hospital in the decade 1948–57. As a special effort is made to secure them in cases of tuberculosis they represent a high proportion of the patients who died of tuberculosis.

A graph shows that in the early years the proportion of cases dying undiagnosed was small, but in the last 5 years it averaged 37%. The explanation is made clear when the age incidence in the 2 halves of the decade is compared. The proportion of those dying when over 50 years of age has risen from 41% to 80%, and as the age rises so does the proportion of undiagnosed cases. The principal tuberculous lesions are tabulated; chronic pulmonary tuberculosis was less frequent but bronchopneumonia cases rose sharply in the second quinquennium. Of the undiagnosed cases 7 had another major disease which masked the tuberculosis though on reassessment the patients were judged to have died of tuberculosis. In 9 cases the diagnoses were not made at necropsy but had to wait for histological examination; these included 2 cases of tuberculous septicaemia, 2 where the bronchopneumonia was considered non-specific, and also cases where miliary tuberculosis was mistaken for disseminated carcinomatosis.

A clinical analysis of the 24 undiagnosed cases where adequate clinical information was available is given. In 14 patients the illness was so far advanced that they lived less than 10 days; this occurred in 5 out of the 6 undiagnosed cases of bronchopneumonia. 3 cases of meningitis in children, all in the first quinquennium, were undiagnosed, though tuberculosis was suspected in 2. There was also 1 case of meningitis in an old woman. Of the others, 4 had tuberculous septicaemia, 4 tuberculous peritonitis and 2 tuberculous pericarditis. No patients with chronic pulmonary tuberculosis died undiagnosed.

This is a valuable and illuminating paper which calls attention to the possibility of tuberculosis as the correct diagnosis in some cases of obscure acute illness in old people.

F. H. Young

LAUCKNER, J. R. **The Treatment of Tuberculosis in the Tropics.** *J. Trop. Med. & Hyg.* 1959, Jan., v. 62, No. 1, 1–9, 7 figs. [11 refs.]

A number of articles on tuberculosis in tropical and undeveloped countries have appeared recently and this one follows the same trend.

In Ibadan, Nigeria, the infection rate is high; by the age of 20 years, 80% are infected, but in the country districts it is thought to be much lower.

A new classification based on the expected response to chemotherapy is suggested; it depends on the estimated percentage of reversible and non-reversible lesions in the patient. In patients treated with PAS and isoniazid for 6 months about 85% of the reversible grades were considered satisfactory irrespective of the extent of the disease, as against 15% of predominantly fibrotic, and 41% of the mixed types respectively. Treatment with isoniazid alone was moderately effective (66%) in the reversible type, but ineffective in the fibrotic. 90% and over were, however, satisfactory in all types when treated by the 3 standard drugs together. The relapse rate in those treated with isoniazid alone was higher. Other forms of tuberculosis were usually treatable with isoniazid alone; the numbers quoted do not merit further details. An alarming rate of resistance, especially to isoniazid, has recently been found in new patients. 30% of 78 cultures showed some degree of resistance to at least 1 of the standard drugs. This is attributed to previous irregular treatment, as it is estimated that 50% of the patients had previously received some drug treatment. The trial of thiosemicarbazones is suggested. The difficulties which are met with and the methods of dealing with them are discussed.

F. H. Young

SMITH, Margaret H. D. & MATSANIOTIS, N. **Treatment of Tuberculous Pleural Effusions with particular reference to Adrenal Corticosteroids.** *Pediatrics.* Springfield, Ill. 1958, Dec., v. 22, No. 6, 1074–87, 4 figs. [37 refs.]

This article dealing with tuberculous pleural effusions in children suggests that these are by no means innocuous. The Bellevue Hospital figures show that in a series of 176 patients 5·1% died of tuberculosis, 5·7% subsequently developed pulmonary tuberculosis, and in 66 patients pleural thickening remained.

6 cases of pleural effusion of proven tuberculous aetiology with full histories are reported in which steroids were given in conjunction with adequate antituberculous drug therapy. In the 5 who were given steroids early (6 to 10 days after the onset of the illness) the pleural effusion cleared up completely in a space of time much shorter than is usual on normal therapy. In the sixth case, steroids were only started about 3 months after the onset of the illness, and no beneficial effect was noted. No patients developed lung or other tuberculous lesions subsequently, but the follow-up period was short. Prednisone was usually given orally every 6 hours in doses totalling 0·5 mgm. per kgm. of body weight in 24 hours (maximum total daily dose 20 mgm.) for 1 to 3 weeks with gradual reduction and cessation after 5 to 6 weeks. No ill effects were noted. The authors recommend the use of steroids as obviating residual pleural thickening and causing rapid clearing of the effusion. A case is made out for a trial on a much larger number of patients.

F. H. Young

GEDDES, J. E. **Group Radiography in Tuberculosis Control.** *Health Bull.* (Issued by the Chief M.O., Dept. of Health, Scotland.) 1959, Jan., v. 17, No. 1, 14–15.

Except under special circumstances general mass X-ray surveys in countries where tuberculous infection has been drastically reduced have become expensive when calculated per new case of active pulmonary tuberculosis discovered. Selected groups are more profitable, but which groups should be selected is not yet decided. This article deals with hospital out-patients.

12% (1,962) of the out-patients at the Western Infirmary at Glasgow in the late summer of 1955 were examined by miniature films during a 2-month period; unfortunately how they were selected is not stated. 11·2 per 1,000 cases of active pulmonary tuberculosis were discovered. This is compared with 3·7 per 1,000 revealed by the Glasgow mass X-ray campaign in 1957 [this *Bulletin*, 1959, v. 34, 426]. During the 18 months which elapsed between the 2 surveys the tuberculosis notification figures had fallen, but the difference is so great that it is felt that hospital out-patients are a very profitable group to submit to routine mass X-ray. The number referred from the various departments is given, but the numbers are too small for analysis. Any experienced worker would expect that a high discovery rate would emerge from those referred from the gastro-intestinal department, and this is confirmed by the discovery of 7·1 per 1,000 cases of active pulmonary tuberculosis in the 622 patients referred from this department. The high percentage (31%) of cases referred from this department makes the total discovery percentage figure rather misleading.

[It is regrettable that in a bulletin from this source the misplacement of a line of the text will lead to considerable waste of time by those reading this interesting paper. The top line of the second column should follow the end of the first half of the first column.]

F. H. Young

DUBOS, R. J. **Progress toward the Standardization of BCG Vaccine.** [Editorial.] *Amer. Rev. Tuberculosis.* 1959, Jan., v. 79, No. 1, 80–82.

One of the important unknown variables in the practice of BCG vaccination is the quality of the vaccine, for owing to mutation the cultures of BCG now used throughout the world are widely different from one another and from the original strain from which all have come. These differences manifest themselves in morphology of colonies, rate of growth and other biochemical activities and in their behaviour both in experimental animals and man.

The quality of the vaccine is also affected by the age of the culture at the time of harvest since young bacillary cells have much greater invasive power than

have older cells. Potency is also affected by duration and conditions of storage.

There is a direct relationship between the numbers of viable BCG cells injected and the intensity of the response elicited *in vivo*, and the viable cell count falls rapidly under unfavourable storage conditions. Moreover different samples taken from the same batch of vaccine can differ profoundly in their viable bacillary population and therefore in biological activity.

The test used most commonly to evaluate a BCG vaccine is the tuberculin test but ability to induce tuberculin sensitivity is not the same thing as ability to induce immunity, and in any case the tests usually carried out are inadequate.

Another test used is the comparison of survival times after infection with virulent tubercle bacilli of vaccinated and control animals "but this technique is most unsatisfactory for theoretic and practical reasons that cannot be described here". Evaluation of the extent of disease in the challenged animals has been widely used, and it has been found that vaccination reduces considerably the severity of the lesions produced in guineapigs by the intracutaneous injection of very small doses of virulent tubercle bacilli.

Studies based on the microscopic enumeration of tubercle bacilli in stained sections and bacillary counts in cultures from various organs have also provided very striking evidence of the protective effect of BCG vaccine. Although these are the findings in experimental animals "it can be surmised from theoretic immunology that the protective mechanisms which limit bacterial multiplication in experimental animals also operate in the human disease".

In view of these facts there is great need for criteria by which to define a good BCG vaccine and particularly for quantitative techniques to measure its protective activity. International and national organizations which finance and operate BCG programmes should see to this. *H. G. Calwell*

GUYE, G. Scarifications cutanées effectuées par un procédé mécanique pour la vaccination antituberculeuse. **[BCG Vaccination by Scarification—a New Instrument]** *Schweiz. med. Woch.* 1959, Jan. 31, v. 89, No. 5, 124–6, 3 figs. (2 coloured).

In spite of being slow, inexact and disagreeable to the patient, scarification continues to be used widely in France as the method of choice for BCG vaccination.

This paper gives an account of a mechanical scarifier designed to take the place of the vaccination lancet. There are photographs of the instrument and the concentric scratches made by it on the skin. Penetration of 1 mm. or 2·5 mm. is provided for by an adjustment and scratches of 3–21 cm. long may be made.

Vaccination is done in the gluteal region; 15–30 seconds after scarification fine drops of sero-sanguinous fluid escape and BCG vaccine (75 mgm./ml.) is mixed with this exudate, left for 2–3 minutes and then covered with a sterile dressing which is removed at 24 hours. The amount of vaccine and the length of the scratches are varied according to age. Recommendations concerning these are given in the paper.

If the vaccinated person has not hitherto been infected by the tubercle bacillus no reaction to vaccination is seen until the end of the third week when the scratches become red and swollen. No special care of the lesion is necessary as there is neither discharge nor suppuration. Regional adenitis is rarely detected, even by the vaccinated person. A flat, white linear scar remains as the sole residuum of the vaccination; keloid formation is unknown.

In the series studied the post-vaccinal tuberculin conversion rate was 98·26% with fresh vaccine, 96·16% with dried vaccine, and the BCG test was positive in all 304 vaccinated persons in whom it was used.

H. G. Calwell

CERF, J. La vaccination B.C.G. sans test préalable au Congo belge. **[BCG Vaccination without Preliminary Tuberculin Testing]** *Ann. Soc. Belge de Méd. Trop.* 1958, Aug. 31, v. 38, No. 4, 639–56, 1 graph. [21 refs.]

The tuberculin test is not an unerring criterion of an individual's tuberculin sensitivity for it may give a positive or negative result according to the kind and dose of tuberculin used. In addition sensitivity may be influenced by such conditions as pregnancy or hypothyroidism, by some of the zymotic diseases and by cortisone. There is also non-specific tuberculin sensitivity.

Immunity to tuberculosis is not the same thing as tuberculin sensitivity although they are often found together; the nature of the anti-tuberculous antibody remains obscure and is probably cellular rather than humoral.

A pre-vaccinal tuberculin test may fail to detect the presence of tuberculosis if the person tested is still in the pre-allergic phase of the primary infection and so, despite all care, he may be vaccinated with BCG at what may be a critical moment in the development of the disease.

The view that strong immunity only exists in the presence of strong sensitivity to tuberculin has been upset by the work of DE ASSIS [this *Bulletin*, 1954, v. 29, 603] in Brazil, who regards sensitivity as the precarious state of an individual who is ill-protected against tuberculosis in contrast to anergy obtained by desensitization, which assures solid immunity.

The problem of the relationship between tuberculin sensitivity and immunity has been elucidated by the use of the BCG test in which skin sensitivity to a suspension of living or killed bacilli is tested. Persons with immunity to tuberculosis react rapidly by redness and swelling and those without immunity react slowly or not at all. In a series examined thus 27% who failed to react to the Mantoux test reacted to the BCG test and were therefore considered to have been already infected by the tubercle bacillus. In the absence of the BCG test they would have been regarded as suitable for BCG vaccination.

On the assumption that the development of post-vaccinal tuberculin sensitivity is a sign of the presence of immunity it has been the practice to do post-vaccinal tuberculin tests. Although a dose of 10 TU was usually sufficient to elicit sensitivity due to natural infection it has usually been necessary to use 100 TU to elicit post-vaccinal sensitivity. [This is not the reviewer's experience; the 10 TU dose will elicit a reaction

in successfully vaccinated persons almost without exception.]

One result of selecting candidates for vaccination by the tuberculin test is that some are vaccinated who are theoretically unsuitable and some are rejected who would benefit from vaccination. If all rigorously scientific precautions were taken before vaccination every candidate would have both a tuberculin and a BCG test and be X-rayed—an impossible achievement in a mass campaign, and even insistence on a tuberculin test is a great obstacle. Therefore since the tuberculin test, in this context, seems to have little validity it appears to Cerf reasonable to dispense with it.

The question of the effect of BCG vaccination on tuberculin reactors has been studied by several workers, of whom one is MANDE [this *Bulletin*, 1954, v. 29, 600]. He is quoted as saying that although the vaccination of a reactor is not attended by any serious complication, such complications as occur generally excite unfavourable psychological reactions both in doctors who witness them and in the public. Cerf remarks that this psychological aspect appears to be less important in the Belgian Congo.

Other authors are quoted as favouring the vaccination of reactors, and Cerf reports a pilot scheme in which 1,750 schoolchildren were Mantoux tested (10 TU), X-rayed and vaccinated with BCG intracutaneously several days later. No harmful effect was seen in any child whether reactor or non-reactor to tuberculin. 145 (13%) of the non-reactors to tuberculin reacted to BCG and 16·6% of the reactors were negative to BCG. The concurrence of sensitivity to tuberculin and insensitivity to the BCG test is relatively rare.

It was found that 20% of the vaccinated non-reactors, all with normal vaccinal reactions, failed to react to 100 TU 2½ months after vaccination although 90% reacted to the BCG test. Failure to react to tuberculin would previously have been regarded as a sign that vaccination had failed. Cerf therefore regards the post-vaccinal tuberculin test as of little value in controlling the results of vaccination.

The course of tuberculin sensitivity was studied in vaccinated reactors and both increase and decrease were seen. Decrease was greatest in the oldest children, which phenomenon Cerf attributes to the fact that natural immunity rises with age and that in a healthy individual tuberculin sensitivity rises to a peak along with immunity and then falls while immunity continues to rise to its maximum. The tuberculous person on the other hand continues to have a high degree of tuberculin sensitivity; anergy occurs in the presence of overwhelming tuberculous disease.

Since 1957 350,000 untested schoolchildren in the Belgian Congo have been vaccinated with BCG without any serious complication. The vaccinal lesion measured 4·75 mm. in the youngest group (where tuberculin sensitivity was least) and 5·5 mm. in the older children. In 50,000 children who were vaccinated in 1957 and re-examined in 1958 there was no instance of gland abscess. Cerf envisages the extension of BCG vaccination without preliminary tuberculin testing to the whole population of the Belgian Congo and Ruanda-Urundi.

H. G. Calwell

VENEREAL DISEASES

DJANG, A., KILCREASE, D. T., MCBREEN, Marion & LELAND, S. J. Los principios y métodos de control de las enfermedades venéreas con especial referencia a las actividades del programa en Nuevo México. **[The Principles and Practice of Venereal Disease Control with particular reference to the Programme Activities in New Mexico]** *Bol. Oficina Sanitaria Panamericana.* 1959, Jan., v. 46, No. 1, 32–8, 2 figs.

The English summary appended to the paper is as follows:—

"The special features of venereal disease epidemiology in New Mexico are presented. The rise of venereal disease morbidity during 1957 is mainly attributable to the increased case finding activities during that period of time. As an expression of the venereal disease control program's effectiveness in New Mexico during the last several years the rate of the first admissions to state mental institutions for all psychoses due to syphilis is lower than the mean Continental United States rate.

"Emphasis has been placed on the primary prevention of venereal diseases in New Mexico by increased health educational activities and other procedures. A new venereal disease program was devised to encourage the cooperation of the private practicing physicians. So far, the experimental project, as measured by the morbidity reporting, is a success.

"The Navajo training program was initiated during 1957 to meet the high venereal disease prevalence rate among the Indian Population.

"A new premarital law went into effect on May 3, 1957.

"A jail survey program, a new mobile unit and three other new programs also initiated during 1957–1958 were the rapid plasma reagin test and unheated serum reagin test, and the mass Frei skin test program."

CAVAILLON. Humanisme et syphilis. **[Syphilis and Humanity]** *Arch. Belges Méd. Sociale, Hyg., Méd. du Travail et Méd. Légale.* 1958, Nov.–Dec., v. 16, Nos. 9/10, 505–20.

This is a long and very remarkable article which can only really be appreciated when read in the original.

Syphilis has not always been a shameful disease; soon after its introduction into Europe it involved the rich as well as the poor, the intellectual as well as the illiterate. The author has no doubt that syphilis appeared in Europe after the return of Christopher Columbus and he scouts the suggestion of the treponematosis of the lama. The history of the spread of the disease and the various names given to it from 1497 on through the centuries are well known to most syphilologists; the various measures taken to combat it are set out in some detail and these vary a great deal according to the different ideas as to its cause and method of spread.

A long list of famous authors, poets, artists, philosophers and others with their views occupies the greater part of this paper; some of the descriptions of the manifestations of the disease as seen in the 15th–18th centuries are appalling to those who only see it as it appears today.

Great names among those who have written on the disease are too numerous for all to be mentioned, but these include Erasmus, Grunbeck, Shakespeare, Rabelais, Montaigne, Montesquieu, Diderot, Voltaire, Rousseau and Bernard Shaw; the number of the great who contracted the disease is legion.

This word picture of syphilis as it occurred in Europe over nearly 4 centuries is a masterpiece and several quotations from the poets are gems of their kind.

T. E. Osmond

MILLER, J. N., BOAK, Ruth A. & CARPENTER, C. M. **Sensitivity of the *Treponema pallidum* Immobilization (TPI) Test. A Function of the Number of Spirochaetes in the Antigen.** *Brit. J. Venereal Dis.* 1958, Dec., v. 34, No. 4, 246–9.

These authors carried out TPI tests using antigen containing 15, 5 and 1 spirochaete per high dry field. Details are given in the text and in 5 tables.

Testing 23 antisyphilitic sera they found that maximum sensitivity was obtained when the antigen contained only 1 spirochaete per field and that 5 per field gave better results than 15 per field.

When a doubtful result was obtained with 5 spirochaetes the test was repeated with 1 spirochaete; when the latter test was negative the original was considered non-specific and due to toxic substances; when it was positive it indicated the presence of immobilizing antibody; when it was doubtful no conclusion could be drawn.

In view of the fact that routine tests using only 1 spirochaete are impracticable the authors recommend the use of 5 spirochaetes.

Thus the sensitivity of the TPI test varies inversely with the number of spirochaetes in the antigen.

T. E. Osmond

GRAM, H. G. Die Spirochätenagglutination im Liquor. **[Spirochaetal Agglutination in Cerebrospinal Fluid]** *Deut. med. Woch.* 1959, Jan. 16, v. 84, No. 3, 109–12, 131–2. [33 refs.]

The author has investigated 740 samples of cerebrospinal fluid with a view to contrasting the results of an agglutination test in which spirochaete antigen of the Behring Co. (*Spirochätenantigen Behringwerke*) was used, with the various well-established diagnostic reactions for syphilis—Wassermann, cardiolipin, Meinicke precipitation and citochol reactions. The sera came from general hospitals and included samples from neurological cases and from infective cases of meningitis.

Among the samples of fluid from established cases of neurosyphilis, there were only 3 negative by the agglutination test and 7 in which it was the only method to give a positive. The citochol reaction was least sensitive and the cardiolipin next in sensitivity to the agglutination test. The apparently false positives occurred in less than 1% of the total cases examined if exception is made of the cases of meningitis. In the latter false positives occurred in a somewhat irregular way with the different reagents but it was notable that the cardiolipin reaction was more liable than the others to give false positives in cases of viral infection.

It is considered, therefore, that this method is a valuable addition to those already in use for the diagnosis of neurosyphilis.

J. W. McLeod

COLLARD, P. & EVANS, A. J. **Smallpox as a Cause of False Positive Reactions to the Kahn Test.** *Brit. J. Venereal Dis.* 1958, Dec., v. 34, No. 4, 256–7.

It has long been known that vaccination against smallpox is liable to cause biologically false positive serum reactions for syphilis but there are few records in the literature of the effect of smallpox itself.

These authors investigated 108 males who were convalescent from smallpox and of these 34 (31·5%) gave positive Kahn reactions; this is compared with an expectation of 8·5% in apparently healthy persons of the same race.

11 of these reactors were followed up; 4 reverted to negative in 3 months and the other 7 in 6–7 months. These patients came from Ibadan where yaws is endemic, but there seems no reason to suppose that the positive Kahn reactions were caused by this disease.

T. E. Osmond

KING, A. J. **Drugs in the Treatment of Syphilis: Parts I and II.** *Brit. Med. J.* 1959, Feb. 7 & 14, 355–7; 431–2. [14 refs.]

This subject is divided into 2 parts, presumably for editorial convenience only.

Treatment may be divided into preventive and curative [there seems to be a third type, "continuation", since it appears doubtful whether one can "cure" late latent, late congenital syphilis, tabes or general paralysis].

Preventive treatment may be given before or after exposure to infection; the former involves broad issues of education, public health administration and complex moral problems; the latter should be called "abortive" treatment and is essentially the same as treatment of early cases of the disease; it is mostly applicable to mass campaigns among backward peoples but is advisable in late pregnancy where the risk of infection has been considerable.

For curative treatment penicillin is the drug of choice; a low serum level over a comparatively long period is the aim. Procaine penicillin 600,000 units daily for 10 days or preferably PAM (procaine penicillin G with aluminium stearate) as a single dose of 2·4 mega units or as injections of 600,000 units every 2nd or 3rd day, or if possible every day [the length of the course is not stated], should cure 95% of early cases. Alternative remedies include benzathine penicillin and benethamine penicillin; both these, especially the latter, are liable to cause pain.

For late syphilis the same types of penicillin are advised; the danger of a Jarisch-Herxheimer reaction is probably exaggerated and attempts to avoid this by the use of very small initial doses usually fail. Total dosage is greater than in early cases; for cardiovascular syphilis not less than 8·4 mega units should be given and the addition of bismuth may help; for neurosyphilis a total dosage of 12·6 mega units is recommended.

Syphilitic pregnant women should be treated by means of a 10-day course as early as possible. For congenital syphilis the dosage should be 200,000 units per lb. body weight spaced over 8–10 days; interstitial keratitis usually reacts well to cortisone but treatment must be continued over long periods—often many months—as relapse is liable to occur.

There is evidence that toxic reactions to penicillin are on the increase and 1–5% of patients may be affected; scratch tests and other sensitivity tests are of doubtful value; a history of a previous reaction negatives further treatment with penicillin. Anaphylaxis should be treated with adrenaline or aminophyline, clearing of the airway and oxygen if necessary; delayed reactions may be controlled by antihistamines and cortisone.

Where penicillin is contra-indicated other antibiotics must be used; of these chloramphenicol, chlortetracyline and oxytetracycline are the most effective but all are poor substitutes for penicillin.

It is stressed that all patients treated for syphilis should be followed up for at least 2 years with periodical blood tests and at least one examination of the cerebrospinal fluid. *T. E. Osmond*

KNIGHT, G. **Results of the Treatment of Gonorrhoea in the Birmingham Clinic.** *Brit. J. Venereal Dis.* 1958, Dec., v. 34, No. 4, 223–6, 7 figs.

Male patients suffering from gonorrhoea treated at the Birmingham clinic were: 1955—444; 1956—858; 1957—1,063; and in January–June 1958—544. Of these 998 were white, 225 Indian or Pakistani and 1,122 West Indians. Thus it is clear that gonorrhoea has been increasing and that all nationalities named are involved. Treatment consisted of 300,000 units procaine penicillin followed by 0·5 gm. sulphathiazole 4 times daily for a week; tests of cure were carried out 1, 2, 3, and 4 weeks after treatment and then monthly for 5 months longer. The percentages of defaulters were 1955—16·2; 1956—15·3 and 1957—16·1. Failures for the 3 years were 3·05, 2·3 and 7·3% respectively; West Indians were most affected.

Recurrences in the first month were 2·1, 4·83 and 4·5%; in the first 3 months 3·0, 7·05 and 6·0%; in the first year 8·1, 12·35 and 9·3% respectively.

The numbers of females with gonorrhoea for the 3 years were 83, 147 and 203, the main increase being in white women. It is clear that gonorrhoea is increasing in Birmingham mainly through lack of success in tracing contacts and the author suggests that cure may be too rapid and too easy. *T. E. Osmond*

OATES, J. K. **Diagnosis of Chronic Prostatitis.** *Brit. J. Venereal Dis.* 1958, Dec., v. 34, No. 4, 250–53. [20 refs.]

Chronic prostatitis has always been with us but appears to have received little attention since the introduction of antibiotics in the treatment of urethritis. At different times various estimates have been made by various observers of the incidence of chronic prostatitis both in healthy persons and in those who have suffered from a previous urethritis; these figures range round about 30–40% of apparently healthy males.

The symptoms have been described as perineal discomfort radiating to the groins or suprapubic region and lumbo-sacral region; pyrexia has been recorded. On rectal examination tenderness, induration and boggy swelling have been noted and it has been claimed that the prostatic fluid contains excess of fibrinolysin and acid phosphatase.

However, it is generally agreed that only an excess of pus cells in the fluid is a proof of prostatitis and that clumping of these cells is good evidence. A trial of counting pus cells was undertaken by this author but discarded as impracticable. He finally decided that an examination of 5 wet specimens by means of dark ground microscopy was the method of choice and that more than 10 cells per 1/12 microscopic field, especially if accompanied by clumping, constituted evidence of prostatitis.

[Many years ago Col. L. W. HARRISON stressed the advisability of cleansing the urethra before taking a prostatic specimen in order to obviate contamination with urethral discharge. Recently a method of diagnosing prostatitis by measuring the projection of the prostate into the rectum has been described (see this *Bulletin*, 1959, v. 34, 125).] *T. E. Osmond*

MILES, R. P. M. **Rectal Lymphogranuloma Venereum.** *Postgraduate Med. J.* 1959, Feb., v. 35, No. 400, 92–6, 3 figs. [11 refs.]

This article reports an investigation of the ano-rectal form of lymphogranuloma venereum occurring in 91 patients, all of whom except 6 were females.

There are 3 phases, proctitis, "prestricture" and established stricture; in the first there may be only proctitis with ulcers and punctate haemorrhages of the rectum; there may be multiple sinuses of the perineum and a recto-vaginal fistula. In the second inflammation is less and the rectal walls show fibrosis and the examining finger is gripped. In the third the stricture may be 2 cm. or 5–7 cm. from the anal margin and the pelvic colon is commonly involved.

Diagnosis is confirmed by the Frei and complement-fixation tests.

Treatment: early cases react well to antibiotics, *e.g.* chloramphenicol, tetracycline or erythromycin 28 gm. over 14 days; in chronic cases antibiotics or sulphonamides combined with gentle dilatation relieve symptoms but in very advanced cases a transverse colostomy followed by excision of the diseased rectum and colon is necessary; the sphincter muscle ring should be preserved.

It is thought that the lesions are due to a reaction of the bowel to certain stimuli, *i.e.* the phenomenon is allergic or anaphylactic.

3 beautifully produced photographs show the condition very well. *T. E. Osmond*

MARMELL, M. **Donovanosis of the Anus in the Male. An Epidemiological Consideration.** *Brit. J. Venereal Dis.* 1958, Dec., v. 34, No. 4, 213–18, 8 figs. [19 refs.]

Out of 61 patients with donovanosis (granuloma inguinale) 51 had lesions of the genitals or groin and

10 lesions around the anus; diagnosis was established by demonstration of the organism in smears stained by the method of Wright or Giemsa.

The 10 cases are described in some detail; all the patients were coloured except 1 and all admitted pederasty except 1.

The lesions mostly had a cauliflower appearance, varied a good deal in size and had been present for a few months to several years before diagnosis.

8 beautifully produced figures illustrate the lesions extremely well.

The literature includes 48 similar cases all but 4 of which admitted pederasty. Thus it seems fairly certain that this condition is a venereal one.

[It would have been interesting to know what treatment was applied and what was the outcome.]

T. E. Osmond

CATTERALL, R. D. **Incidence of Chronic Genital Infection in Male Patients with Uveitis. A Preliminary Report.** *Brit. J. Venereal Dis.* 1958, Dec., v. 34, No. 4, 254–5.

This article reports an investigation of 85 patients suffering from uveitis, of whom 74 were followed up; 58 (78·4%) had chronic prostatitis, 17 (22·9%) had Reiter's disease, 8 (10·8%) had ankylosing spondylitis, 2 (2·7%) had plantar fasciitis and 16 (21·6%) had sacroiliitis; thus of 58 patients with prostatitis and uveitis 27 (46·6%) had other metastatic involvement. Cultures were not very helpful; PPLO were grown in 10% of 70 cases; CF tests with PPLO antigen were positive in 20%. It is concluded that PPLO do not play a significant role and the causative organism remains unidentified. *T. E. Osmond*

OTHER COMMUNICABLE DISEASES

The order of papers in this section is as follows: Tetanus; other diseases.

RIIS, P. Tetanus og ulcus cruris. [**Tetanus and Chronic Ulcers of the Legs**] *Nordisk Med.* 1958, July 24, v. 60, No. 30, 1048–9. English summary.

Among 88 patients treated for non-neonatal tetanus in the Blegdams-hospital in Copenhagen between 1940 and 1957 varicose or other ulcers of the leg were the portal of entry in 10 instances. Treatment was by excision, the administration of tetanus antiserum and vaccine, and prolonged narcosis. Toxigenic strains of *Clostridium tetani* were isolated from the ulcers in 6 patients; 2 patients died. The author concludes that chronic ulceration of the legs carries a risk of infection with *Cl. tetani*, and recommends that patients suffering from this condition should be immunized against tetanus. *D. J. Bauer*

FOURRIER, A. et CABANEL C. Les Aspects du Tétanos en Algérie (á propos de 49 cas observés en 16 mois). [**Aspects of Tetanus in Algeria (with regard to 49 cases observed in 16 months).**] *Algérie Méd.* 1957, v. 61, No. 5, 577–93, 2 figs.

This is a survey of the problems of tetanus in Algeria based on a study of 49 cases observed between October 1955 and February 1957. There were 20 cases of umbilical tetanus in neonates, 17 of generalized tetanus in children and 12 in adults. The aetiology of umbilical tetanus lies in the unhygienic midwifery; much of the tetanus in children is due to the habit of walking with bare feet. Of the 20 patients with umbilical tetanus, 18 died; 11 of the 17 children with tetanus died and 5 of the 12 adults. Treatment followed the usual lines with antitoxin, sedation, penicillin and careful nursing and feeding. In 6 patients tracheotomy was carried out and 4 of these survived. Curarization with controlled respirations was done in 2 patients, both of whom died. The only hope of improving the position lies in mass immunization against tetanus.

A. B. Christie

VELASCO-JOVEN, Emiliana, TAN, D. T. D. & DE JESUS N. **Erythromycin as an Adjunct in the Treatment of Tetanus. Report of 100 cases.** *J. Philippine Med. Ass.* 1958, Aug., v. 34, No. 8, 473–80, 4 figs. [10 refs.]

Erythromycin, to which *Clostridium tetani* is sensitive at a minimum concentration of 0·05 micrograms per ml., was given to 100 patients suffering from tetanus. Antitetanic serum 40,000 to 60,000 units intravenously was also given to each patient along with treatment (not specified) to control spasms and cardiorespiratory failure. 21 of the patients were classed as severely ill and 12 died, 33 were moderately ill and 4 died; 46 had mild tetanus and all recovered. The mortality for the 100 patients was thus 16% and the authors claim that this is "comparatively lower than observations abroad".

A. B. Christie

COLLIPP, P. J. & KOCH, R. **Cat-Scratch Fever associated with an Osteolytic Lesion.** *New England J. of Med.* 1959, Feb. 5, v. 260, No. 6, 278–80, 4 figs. [12 refs.]

This is a report on a "case of cat-scratch fever coincident with a granulomatus osteomyelitis of the femur". In only 1 of the approximately 600 cases of the disease which have been recorded previously has this association with a "sterile osteolytic lesion" been observed.

The patient, a 4-year-old boy who had often played with and been scratched by cats, complained of pain in the right knee and was found to have slight fever. A maculopapular eruption was noted and subsequently a swollen cervical node appeared on the left side. After 9 days he was admitted to hospital where the cat-scratch skin test was found to be positive. The cervical node continued to enlarge and become fluctuant. Pus which was sterile was surgically drained from the abscess and an antigen prepared from it caused a strong positive reaction in a known case of cat-scratch fever.

The lymphadenitis subsided but the boy continued to have pain in the right knee and a limp. On the 28th hospital day X-rays revealed an osteolytic lesion in the right femoral intertrochanteric area. Needle biopsy material from this area was sterile but on microscopical examination granulomatous appearances compatible with cat-scratch fever were observed. The boy improved and during the next 5 months the gait became normal and X-rays demonstrated progressive healing of the lytic area. There are 4 illustrative photographs of the bony changes and the microscopical appearance of the biopsy material. *M. E. Delafield*

ZOONOSES

In this section the abstracts are arranged as far as possible in the following order: General; Anthrax; Brucellosis; Tularaemia; Leptospirosis; Ornithosis; Others.

For such tropical diseases as Trypanosomiasis, Leishmaniasis, Rickettsial Fevers, Yellow Fever, Plague, etc., see TROPICAL DISEASES BULLETIN.

AWAD, N. A. **Serum Protein Electrophoresis in Brucellosis.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1959, Jan., v. 53, No. 1, 83–90. [21 refs.]

The author studied the serum protein electrophoretic pattern in guineapigs experimentally infected with *Brucella abortus* and in a few human patients suffering from *Br. melitensis* infection. The experimental work was well controlled. 2 types of experiment were performed. In the first a batch of guineapigs shown by negative blood culture and agglutination to be free from brucellosis were injected intramuscularly with a standardized dose of *Br. abortus* and infection was subsequently confirmed by recovery of the organism from the blood or the development of sero-agglutinins in dilutions of between 1 :320 to 1 : 2,560. In the guineapigs which survived serum protein electrophoresis was carried out initially and at 4, 8 and 12 weeks after infection. In the second experiment 1 of 2 comparable batches of uninfected guineapigs was injected with *Br. abortus*, the other batch was kept as a healthy control group and blood examined from both groups as in the first experiment. The experiments both showed that there was little change in the level of the total serum proteins but that the albumin fraction became progressively decreased as the disease became chronic. There was a progressive rise in the gamma globulin fraction while the albumin-globulin ratio showed a progressive fall. The alpha-globulin fraction rose during the acute stage but later returned to normal, the beta-globulin showed a change in the opposite direction. It is suggested that the increase of gamma-globulin is related to increased antibody formation and increased mesenchymal activity with hyperactivity of plasma reticulum.

The author states that similar changes were found in the human infections but details are not given.

[A well-controlled animal experiment but recorded evidence in human infections would be desirable, see *idem* this *Bulletin*, 1959, v. 34, 220.] *Frederick J. Wright*

LOSTIA, G. B. & NERI, W. Risultati di alcune indagini epidiologiche sulla brucellosi in Provincia di Parma. **[Epidemiological Investigations on Brucellosis in the Province of Parma.]** *Igiene Moderna.* 1958, July–Aug., v. 51, Nos. 7/8, 499–510. [18 refs.] English summary.

An increase of human brucellosis in Parma giving an incidence of 22·1 cases per 100,000 a year throughout 1952–6 compared with an incidence of 15·8 cases a year in 1947–51, mainly marked in the plains in contrast with hill and mountain areas, prompted this investigation carried out in 1955, 1956 and the first half of 1957, by the Hygiene Institute of the University of Parma and by the hygiene and prophylaxis laboratory of the province.

Agglutination tests and, in early cases, blood cultures were carried out on patients and on contacts who showed any signs of illness. Milk from cows which had any connexion with the case was examined by the ring test and culturally, and agglutination tests on blood serum were also carried out. The medium used contained tryptose agar, actidione, polymyxin B, bacitracin and ethyl violet. 193 of 208 human cases were studied. They all had a positive agglutination reaction (no titres given); blood cultures were made in 33 cases of which 7 were positive. 934 cows were examined, most by the ring test, some by testing for serum agglutinins, and some in both ways. In 395 animals one of these tests at least was positive. Only 9 of 72 cultured samples of milk were positive. Typing was carried out on these and on the 7 human strains: all had the general characteristics of *Brucella melitensis* and the serological behaviour of *abortus*, which puts them in the *Br. intermedia* species.

The close connexion of human incidence with disease in animals is apparent, and the increase of brucellosis in human beings appears attributable to an increase in the bovine population, there being 250,000 head of cattle in the province, of which 115,000 are milking cows; there are only 15,000 sheep and goats. In rural areas incidence is almost completely limited to persons who have to do directly with cattle; this is remarkable considering that all the inhabitants of such areas consume milk, butter and cheese deriving from infected herds. The authors tentatively attribute this to the very widespread habit of boiling milk and to the use of bulked supplies (which, they suppose, could decrease the number of bacteria by dilution). It also appears possible that bacteria are passed in the milk only for a short period after abortion. In butter, it seems, there is no actual bacterial increase. *E. Agius*

VANINI, G. & BOMPANI, R. Comportamento *in vivo* ed *in vitro* dell'eritromicina su *Brucella.* **[Erythromycin activity on *Brucella in vivo* and *in vitro*.]** *Igiene Moderna.* 1958, July–Aug., v. 51, Nos. 7/8, 584–94. [20 refs.] English summary (6 lines.)

The action of erythromycin on brucellae was studied by *in vitro* tests, by its effects on infected guineapigs,

and by the treatment of 32 human cases naturally infected with brucellae which were said to be *Br. intermedia.*

In vitro the activity of erythromycin was compared with that of Achromycin [tetracycline], terramycin, aureomycin and chloramphenicol. It appeared to be second best after Achromycin. Guineapigs were infected either with *Br. melitensis* or with *Br. abortus*, the infecting dose being 20,000 micro-organisms. Treatment consisted in 0·5 mgm. daily which was started on the tenth day after infection and kept up for 10 days. The animals were observed for 60 days. Only in 1 case, infected with *Br. abortus*, was the micro-organism recovered post-mortem, brucellae being cultivated from all the controls. There were no differences in agglutinin titres and in the opsonic indexes between treated and control animals.

Human patients were treated with 1 to 1·5 gm. per day, being given 250 mgm. every 4 or 6 hours. Most of the patients received a total of 30 gm. The temperature generally fell to normal within 4 to 7 days; in 24 cases the blood became sterile by the sixth day, while in others sterility was attained within the second week of treatment. The agglutinin titres and opsonic indexes were not affected and the drug was well tolerated. There were 9 relapses, which responded to a second course of erythromycin. In view of this tendency to relapse the authors advise that intravenous vaccine therapy should be used jointly with antibiotics.

E. Agius

Szyfres, B., Blood, B. D. & Moya, V. Estado actual de la brucelosis en la América Latina. [**Status of the Brucellosis Problem in Latin America**] *Bol. Oficina Sanitaria Panamericana.* 1959, Jan., v. 46, No. 1, 48–64. [103 refs.] English summary.

Vershilova, P. A. & Golubeva, A. A. **Dermal Revaccination against Brucellosis among Workers in Meat Combines and in Cattle-Breeding Stations.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, Nos. 3/4, 391–6. [Translated from Russian.]

This is an account of the reactions of groups of workers in the meat trade in many areas of Russia to vaccination against brucellosis with a concentrated live vaccine given by the dermal route. 7,125 persons were inoculated, and an analysis of the reactions in 2,263 showed that general reactions occurred in 5·3%, which, however, were not severe. Local reactions occurred in most cases, but were not severe. One of the advantages claimed for this method of vaccination is that it can be carried out even although the person to be immunized shows evidence of allergic sensitivity to the *Brucella* products.

Data are quoted indicating considerable protection in vaccinated groups and a high incidence of infection among their fellow workers who were uninoculated. No comprehensive figures covering the whole group of vaccinated and their unvaccinated comrades are given, however.

J. W. McLeod

Held, J. R., Bauer, H. & West, R. L. **Effect of eradicating Brucellosis in Cattle on Incidence of Human Cases.** *Pub. Health Rep.* Wash. 1958, Dec., v. 73, No. 12, 1096–1100, 4 figs.

This report gives a statistical survey of brucellosis in Minnesota which had a human population showing a steady rise from 2·51 million in 1927 to 3·25 million in 1956. In 1939 the Minnesota Legislature enacted a law authorizing the State Livestock Sanitary Board to control and eradicate bovine brucellosis according to an area plan which made participation obligatory. After blood testing of cattle, slaughter or isolation of infected animals is carried out and importation of cattle is controlled. The milk ring test and vaccination of calves are only considered to be supplementary measures. As a sequel an increasing number of counties has been yearly "certified" [presumably as free from infection]. From 1927 to 1946 the number of cases of human brucellosis notified annually increased from 6 to 403. Since that date there has been a steady fall to 63 in 1956, the case rate per 100,000 falling from a maximum of 13·84 to 1·94. From 1927 to 1948, as the number of cattle became larger or smaller the incidence of human brucellosis showed a corresponding change; since 1949 this relationship no longer holds. The case rates in non-certified counties remain higher than in certified counties (except in 1956 which is attributable to a migration of population). The predominant organism recovered on blood culture from human infections was *Brucella abortus*, supporting the view that cattle are the main source although *Br. suis* and *Br. melitensis* have also been found in man.

[The authors make no allowance for the effect of compulsory pasteurization since 1949 and minimum standards for Grade A milk being legally applied from 1952, but these laws presumably apply to both certified and uncertified counties. The occupations of those notified as suffering from brucellosis are not recorded. If the milk consumed is safe, the incidence of the disease would presumably be predominantly in veterinarians, farmers and milkers having contact with the organisms before pasteurization. (See Pop *et al.*, this *Bulletin*, 1958, v. 33, 843.)] *Frederick J. Wright*

See also p. 582, Drozhevkina, *Brucella* **Bacteriophage and the Prospects of its Utilization.**

Galton, Mildred M. **The Epidemiology of Leptospirosis in the United States.** *Pub. Health Rep.* Wash. 1959, Feb., v. 74, No. 2, 141–8, 3 figs. [49 refs.]

Bence, J. J. & Miller, N. G. **A Serologic Survey of Leptospirosis in a Nonselect Group of Hospital Patients and in Packing House Workers.** *Amer. J. Hyg.* 1958, Sept., v. 68, No. 2, 120–25. [21 refs.]

The sera of 528 unselected patients in hospitals in Omaha, U.S.A. were tested for the presence of leptospiral agglutinins against *Leptospira canicola, L. icterohaemorrhagiae* and *L. pomona.* Titres of 1/100 for *L. pomona* were found in 2 sera; of 1/30 in 2 others; and of 1/30 for *L. icterohaemorrhagiae* in another 3.

None contained antibodies for *L. canicola.* In a similar survey on 233 workers in a meat-packing establishment, 12 sera had titres of 1/100 or higher, and 3 of 1/30 for *L. pomona.* One serum which reacted to 1/3,000 with *L. pomona* and also agglutinated *L. icterohaemorrhagiae* to 1/1,000 was probably from a recent case. No other serum reacted with *L. icterohaemorrhagiae* or with *L. canicola.* These findings again emphasize the importance of occupational factors in the epidemiology of leptospirosis. *J. C. Broom*

VAN RIEL, J. & GASPART, P. Premiers cas humains d'infection par *Leptospira grippotyphosa* en Belgique. [**First Human Cases in Belgium of Infection with** *Leptospira grippotyphosa*] *Bruxelles-Méd.* 1958, Nov. 16, v. 38, No. 46, 1889–93.

The first of the 2 patients described in this report developed a mild febrile illness, but jaundice appeared on the 5th day and was accompanied by diminution in the secretion of urine. The man, aged 38, was admitted to hospital in a stuporous condition and, although the oliguria was not marked, the blood-urea level continued to rise and reached 350 mgm. per 100 ml. on the 12th day. He collapsed suddenly and died on that day, probably as the result of severe internal haemorrhage. Guineapigs injected with blood and urine did not become infected, but the patient's serum had an agglutinin titre of 1/1,000 for *Leptospira grippotyphosa.*

In the second case also the diagnosis was confirmed by serological tests, but the patient was not treated by the authors. It is known, however, that the man, a soldier, developed jaundice and died of the attack.

Both men had been angling in rivers a week or so before the onset of illness, and the authors suggest that they may have been infected through contact with water contaminated with leptospires. *J. C. Broom*

POKORNÝ, B., LEHKÝ, F., ŠEBEK, Z. & VOSTA, J. Weitere neue Leptospirenträger in Böhmen. [**Additional New Animal Carriers of Leptospira in Bohemia**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, Nos. 1/2, 135–41, 2 figs. [13 refs.]

As part of an investigation of the incidence of leptospirosis in southern Bohemia, serological tests and cultural and histological examinations of kidney material were made from 118 common shrews (*Sorex araneus*) 73 musk rats (*Ondatra zibethica*) 50 water voles (shown as *Wasserratten, Arvicola terrestris* [? *amphibius*]) and 24 water shrews (*Neomys fodiens*). The results are shown in the table [which is a shortened version of one given by the authors]. The single strain isolated in culture proved to be *Leptospira grippotyphosa,* and all the positive sera reacted only with that serotype.

Agglutinins, almost invariably for *L. grippotyphosa,* were demonstrated in the sera of a wide variety of species of both herbivores and carnivores. The authors hesitate to draw conclusions about the significance of these findings because cultural and histological examinations were either negative or could not be carried out for technical reasons. [Reports of previous investigations of leptospirosis in Bohemia were given by HAVLÍK *et al.* and by ŠEBEK, this *Bulletin,* 1958, v. 33, 232.] *J. C. Broom*

New Reservoirs of Leptospires in Bohemia

Species and No. examined	Positive agglutinins	Positive kidney section	Positive kidney cultures
Sorex araneus (118)	8	4	1
Ondatra zibethica (73)	6	5	not done
Arvicola terrestris (50)	6	4	0
Neomys fodiens (24)	2	1	0

i. MCKEEVER, S., GORMAN, G. W., GALTON, Mildred M. & HALL, Anna D. **The Raccoon,** *Procyon lotor,* **a Natural Host of** *Leptospira autumnalis. Amer. J. Hyg.* 1958, July, v. 68, No. 1, 13–14.

ii. MCKEEVER, S. GORMAN, G. W., CHAPMAN, J. F., GALTON, M. M. & POWERS, D. K. **Incidence of Leptospirosis in Wild Mammals from Southwestern Georgia, with a Report of New Hosts for Six Serotypes of Leptospires.** *Amer. J. Trop. Med. & Hyg.* 1958, Nov., v. 7, No. 6, 646–55, 1 fig. [19 refs.]

i. Strains of leptospires were isolated from 18 of 281 raccoons trapped in Grady County, Georgia, U.S.A. and of the 13 strains which have been identified 7 proved to be *Leptospira autumnalis.* 6 of the animals were caught in stands of bottomland hardwood along small streams which are ideal habitats for raccoons. The epidemics of Fort Bragg fever, shown retrospectively to have been caused by *L. autumnalis* [GOCHENOUR *et al.*, this *Bulletin,* 1953, v. 28, 115], occurred among soldiers quartered near a small stream where the vegetation was predominantly bottomland hardwood. Raccoons were numerous in the area, so contamination of the stream may have been the cause of these epidemics.

ii. Leptospires were isolated in culture from the kidneys of 44 of 820 mammals, representing 14 species, trapped alive in various districts of South-Western Georgia, U.S.A. 2 strains failed to survive, and 3 others are not yet fully classified. The identities of the others were as follows: *Leptospira australis A* (2 strains), *L. ballum* (16), *L. grippotyphosa* (2), Hebdomadis serogroup (2), Hyos serogroup (4) and *L. pomona* (13). The following new host records were established: *Didelphys marsupialis* (opossum) for a member of the Hyos serogroup; *Mephitis mephitis* (striped skunk) for *L. ballum* and *L. pomona*; *Procyon lotor* (raccoon) for *L. australis A, L. ballum, L. grippotyphosa, L. pomona* and a member of the Hebdomadis serogroup; *Urocyon cinereoargenteus* (grey fox) for *L. ballum.*

The authors regard the identification of *L. australis A, L. grippotyphosa* and members of the Hebdomadis and Hyos serogroups as being of special importance. These serotypes have not normally been included in routine leptospiral agglutination tests up to the present so human and animal infections caused by them may have been missed. [This article contains a useful summary of the methods used to obtain the material for this

survey, and should be consulted by any workers who intend to carry out a similar piece of work.]

J. C. Broom

RUSSELL, R. W. R. **Treatment of Leptospirosis with Oxytetracycline.** *Lancet.* 1958, Nov. 29, 1143–5. [21 refs.]

A controlled clinical trial was carried out of the value of oxytetracycline in treatment of leptospirosis contracted by 52 servicemen during jungle duties in Malaya. The diagnosis was confirmed in all cases by blood-culture or serological tests and alternate patients were placed in the treatment (27) and control (25) groups. Treatment was begun as soon as a provincial diagnosis was made, and consisted of an initial dose of 1·5 gm. oxytetracycline followed by 0·5 gm. every 6 hours for at least 5 days or until the temperature had been normal for 48 hours.

If the drug caused severe vomiting, so rendering oral therapy impossible, 1·0 gm. dissolved in a pint of glucose-saline was given intravenously, being run in slowly over 8 hours. 3·0 gm. were given in the first 24 hours and 2·0 gm. daily for as long as intravenous administration was necessary.

Patients in the control group received 50 mgm. ascorbic acid 3 times a day as a placebo. The duration of the illness was calculated in 2 ways: (1) from onset until the temperature became normal; and (2) the duration of symptoms after treatment was begun. In the control group the averages were 9·4 days' pyrexia and 6·9 days' duration of symptoms; in the treatment group the corresponding figures were 6·4 days and 4·0 days.

It appears that oxytetracycline therapy can shorten both the period of fever and the duration of symptoms. It did not, however, prevent renal and hepatic complications because in 6 of the treatment group the blood urea level rose after therapy was started, and 6 developed jaundice compared with 7 and 5 respectively in the control group.

[The value of penicillin in treatment of leptospires among troops in Malaya was reported by MACKAY-DICK and ROBINSON, this *Bulletin*, 1958, v. 33, 344.]

J. C. Broom

MENGES, R. W. **Control of Leptospirosis in Man and Animals.** *Pub. Health Rep.* Wash. 1959, Feb., v. 74, No. 2, 149–52. [24 refs.]

MOHR, W. Über das Vorkommen der Maul-und Klauenseuche beim Menschen. [**The Occurrence of Foot and Mouth Disease in Man**] Reprinted from *Landarzt.* 1958, Sept. 20, v. 34, No. 26, 845–8.

Diseases due to Fungi

For papers on systematic mycology, see the section in Bacteriology, below. Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN

MAIN, P. T. **Ringworm contracted from Cattle: a Two Years' Survey in General Practice.** *Practitioner.* 1959, Mar., v. 182, No. 1089, 347–54. [14 refs.]

31 cases of cattle ringworm were diagnosed during a 2-year period in a rural practice of approximately 2,000 patients in Sussex, England.

The fungus usually responsible was *Trichophyton discoides* and 90% occurred in farm workers and their families. The condition was more common among males and there was a higher incidence of infection during the winter months. Man-to-man infection was common. A number of different forms of treatment were used and it seemed that almost any form of fungicidal preparation cleared up the lesions if treatment was carried on for long enough and the lesions covered. However, the clinical course was often prolonged.

It is emphasized that closer cooperation is needed between the veterinary and medical professions to work out methods of controlling the disease. *Peter Abbott*

CREMER, G. Onderzoek naar de verspreiding van voetmycosen te Amsterdam. [**Incidence of Tinea Pedis in Amsterdam**] *Nederl. Tijdschr. v. Geneesk.* 1959, Feb. 28, v. 103, No. 9, 448–52. [10 refs.]

The English summary appended to the paper is as follows:—

"In order to gain an insight into the incidence of tinea pedis among the population of Amsterdam, 101 students, 212 nurses, 268 labourers and 313 children aged 2–14 were examined; of these groups 28, 20, 31 and 0–8 per cent. respectively were affected. Among students the incidence of tinea pedis had increased by 100 per cent. in just over 20 years. In only one third of all cases interdigital lesions proved to be of mycotic origin. Growth on Littman agar was obtained 119 times, viz., *Trichophyton mentagrophytes* 93, *Trichophyton rubrum* 23 and *Epidermophyton floccosum* 3 times. In contrast with the relative statistics of the outpatient department, *Trichophyton mentagrophytes* was far more frequent than *Trichophyton rubrum.* Among

15 adults with hyperhidrosis only one had tinea pedis. Familiar infection is discussed and some instances are given."

SANDS, J. H., SCHULZ, D. M. & AROMSTAM, E. M. **The Indeterminate Pulmonary Infiltration—Our Diagnostic Dilemma. Report of Twenty-Three Cases of Chronic Granulomatous Disease of the Lung.** *Arch. Intern. Med.* 1959, Jan., v. 103, No. 1, 23–7.

23 cases of granulomata of the lung, presenting as indeterminate pulmonary infiltration, are analysed.

X-ray appearances and the results of skin tests, complement-fixation studies, bronchoscopy and in some cases sputum cultures and cultures from excised tissues were evaluated and led to the diagnosis of histoplasmosis in 11 cases and blastomycosis, coccidioidomycosis and cryptococcosis in 2 each. 5 remained as clinical granulomata of unknown aetiology and 1 showed an unidentified mycelium-forming fungus.

The authors emphasize the lack of a characteristic roentgenographic picture which will distinguish the fungous infections of the lungs from other granulomata such as tuberculosis or neoplasm. They point out the deficiencies of the skin and complement-fixation tests though they consider them valuable adjuncts in differential diagnosis and they make a plea to clinicians to exhaust all available diagnostic methods, including surgery, before committing any patient to a long programme of treatment such as that required for tuberculosis.

"An aggressive surgical approach and better histopathologic, cultural and serologic methods are all greatly needed in our quest for an accurate diagnosis of the indeterminate pulmonary infiltrations."

Peter Abbott

SEIDES, S. W., BOIES, L. R., Jr. & MALAWISTA, S. E. **Histoplasmin, Tuberculin, and Coccidioidin Skin Sensitivity in Liberian Aborigines.** *Amer. J. Trop. Med. & Hyg.* 1959, Jan., v. 8, No. 1, 37–40. [17 refs.]

"1. The incidence of skin sensitivity to histoplasmin among 712 working Liberian males was found to be 18.1 per cent and among 66 school children 3.0 per cent. Of the tested population 4.4 per cent showed positive reactions at only one of the two readings taken. Distribution of reactivity among 16 Liberian tribes is presented.

"2. The incidence of positive tuberculin tests among 1,031 working Liberian males was 74.7 per cent, and among 248 school children 38.3 per cent. Of the total tested population 6.6 per cent reacted positively at only one reading. There was no significant cross reactivity between the histoplasmin and tuberculin agents used.

"3. The incidence of positive skin tests to coccidioidin in 733 subjects was 1.2 per cent."

LOURIA, D. B., FEDER, N., MITCHELL, W. & EMMONS, C. W. **Influence of Fungus Strain and Lapse of Time in Experimental Histoplasmosis and of Volume of Inoculum in Cryptococcosis upon Recovery of the Fungi.** *J. Lab. & Clin. Med.* 1959, Feb., v. 53, No. 2, 311–17.

"The present experiments show that the time interval between inoculation and sacrifice was important in the recovery of some strains of *H. capsulatum* from liver and spleen of mice used in experimental studies. The optimum interval was 2 weeks. Increasing the interval to 8 to 14 weeks decreased the proportion of positive cultures of certain strains. A uniform decrease was not apparent in some recently isolated strains. No decrease in positive cultures was noted upon increasing the interval between inoculation and sacrifice after infection with *C. neoformans*. When mouse inoculation is used as a method of diagnosing suspected fungal disease, it is suggested that several mice be sacrificed 2 weeks after intraperitoneal injection of specimens possibly infected with fungi, and that additional mice be sacrificed 4 to 8 weeks after inoculation.

"Evidence is also presented indicating that culture of a large volume of spinal fluid is an important factor in the isolation of *C. neoformans* from some patients with cryptococcal meningitis. It is suggested that at least 20 ml. of blood, urine or exudate, and a minimum of 5 ml. of spinal fluid be cultured when conventional cultures for fungi are negative in a patient suspected of harboring a mycotic infection."

Cancer

LINDSEY, A. J.; SMYTH, C. N. **Tobacco Smoke.** [Correspondence.] *Brit. Med. J.* 1959, Feb. 21, 506–7, 1 fig.

Dr. Lindsey tabulates the amount of each of 8 hydrocarbons found in smoke and unsmoked stubs resulting from mechanically smoking 100 cigarettes to a stub length of 15 mm. and 100 to a stub length of 35 mm. The smoke from the former contained more of each hydrocarbon, except anthracene, than that from the latter. Of specific interest are the carcinogenic hydrocarbons, 1:2-benzanthracene and the more active 3:4-benzpyrene; 14·0 and 8·0 μgm. of the former and 3·0 and 0·7 μgm. of the latter were found after smoking to the shorter and longer stub lengths respectively. The stubs retained considerable amounts of the hydrocarbons. The shorter stubs contained more of the compounds of heavy molecular weight than the longer

stubs; thus there were 36·0 μgm. of fluoranthene and 11·0 μgm. of coronene in the 15 mm. stubs compared with 12·0 and 0·4 μgm. respectively in the 35 mm. stubs. It is suggested that the compounds of lighter molecular weight are liable to more destruction during the repetitive distillation that takes place during smoking. In the longer stubs there were 42·0 μgm. of anthracene, 0·7 of anthanthrene, 3·0 of 3:4-benzpyrene and 14·0 of 1:2-benzanthracene, compared with 12·0, 0·3, 2·0 and 8·5 μgm. respectively in the shorter stubs. These results support the suggestion of DOLL, HILL, GRAY and PARR [this *Bulletin*, 1959, v. 34, 444] that small differences in stub lengths might result in substantial differences in the amounts of inspired carcinogens.

Mr. Smyth comments on some aspects of Wynder's review [*ibid.*, 443] of laboratory investigations on the "tobacco and cancer relationship" and suggests that the total tar inspired during cigarette smoking could be reduced by better ventilation of the cigarette stub. He presents diagrammatically the trend of smoke and stub temperature during the course of smoking "average English cigarettes" (normal) and cigarettes with 2 needle pricks of 0·64 mm. diameter at 12·7 mm. from the "mouth end" (treated). It is stated that such ventilation can decrease total tar extraction by 60% in cigarettes smoked to a stub length of 15 mm. The stub temperature, measured at about 6 mm. from the mouth end, of treated cigarettes was 62°C. cooler than normal when all but 15 mm. had been smoked. The temperature of emerging smoke when the same amount of cigarette had been smoked was some 56°C. cooler in treated than in normal cigarettes. Material differences between treated and normal cigarettes start to appear in stub temperatures at a stub length of about 25 mm. and in smoke temperatures when slightly less of the cigarette has been smoked. Although no data are given it is said that increasing the number of air inlets near the stub probably diminishes temperatures still further as they reduce the power of each draw to brighten the burning end. *E. A. Cheeseman*

KORTEWEG, R. **Mortality from Tobacco.** [Correspondence.] *Brit. Med. J.* 1959, Mar. 7, 645.

"In the first half of 1958 I made a similar investigation in the Netherlands. Cigarette butts from a restaurant, an office, a railway station, and from canteens for officers and for laboratory personnel were collected and measured after the method of Hammond in the U.S.A.

* * *

Comparison of Cigarette Ends Measured in the Netherlands, U.S.A., and England and Wales

Lengtn of Butt (mm.)	Non-filter Cigarettes		All Cigarettes (Filter and Non-filter)		
	U.S.A. (%)	Netherlands (%)	U.S.A. (%)	Netherlands (%)	England and Wales (%)
Up to 9·5	1·8	2·0	8·0	1·8	1·2
10–14·5		15·2 17·2		13·8 15·6	17·5 18·7
15–19·5	7·6	31·5	7·9	32·4	46·7
20–24·5	17·1	28·8	19·7	28·7	25·4
25–29·5	22·1	13·2	19·9	13·0	6·9
30–34·5	21·8	4·9	20·9	5·3	1·4
35–39·5	12·6 51·6	2·6 9·3	12·8 51·7	2·9 10·3	0·6 2·3
40+	17·2	1·8	18·0	2·1	0·3
Total butts measured	1.697 (100%)	798 (100%)	4,283 (100%)	890 (100%)	772 (100%)
Average length (mm.)	30·7	20·5	30·9	20·8	18·7

* * *

"Our conclusion is, therefore, that the Dutch investigation adds new evidence to the suggestion that the habit of throwing away a large unsmoked butt may contribute to the relatively low mortality from cancer of the lung in the U.S.A."

Dental Hygiene

GARCELON, A. H. **Five Years' Experience with Fluoridation in Norway, Maine.** *New England J. of Med.* 1959, Jan. 15, v. 260, No. 3, 127–9.

The town of Norway, Maine, began fluoridation of its water supply in October, 1952. About that time, 191 children, 6–14 years old, were dentally examined, and a similar examination was carried out in 1957. During that period the average number of decayed, missing and filled permanent teeth was reduced by more than one-half among children aged 6–9 years, by more than one-quarter among those aged 10–12 years, and by about one-tenth among those aged 13–14 years.

During the same period the percentage of children aged 6–9 years who were entirely free from dental caries in permanent teeth more than doubled—the actual percentages being 18·0 in 1952 and 39·1 in 1957. There were not sufficient caries-free children in the 10–12 years age-group to warrant any conclusions regarding an increase of freedom from caries in that group.

The maximum benefits of fluoridation occur when the fluoride is incorporated in the tooth enamel while it is being formed and, consequently, the younger children who had more of their teeth formed during the fluoridation period received greater benefit than did the older children. *Robert Weaver*

Occupational Hygiene

In this section the abstracts are arranged as far as possible in the following order : General; Mining and Dust Diseases; Poisoning due to Metals, Solvents and Other Substances; Skin and Other Affections; Radio-Active Substances; Other Conditions; Occupational Psychology

MEIKLEJOHN, A. **i. Industrial Health—Meeting the Challenge.** *Brit. J. Indust. Med.* 1959, Jan., v. 16, No. 1, 1–10. [10 refs.] **ii. Outbreaks of Fever in Cotton Mills at Radcliffe, 1784.** [Miscellanea.] *Ibid.* 68–9, 1 fig.

I. The modern industrial system originated in England just over 200 years ago, when the introduction of machines led to a change from the domestic to the factory system of manufacture and trade. The critical advance was in the engine which generated power in a fixed place, with the consequence that the workpeople were crowded into one building, and, if they had no other homes, lived in it.

The picture of the industrial revolution, with its child labour, is well known. The author, in this MacKenzie Industrial Health Lecture, shows that the outbreaks of infectious disease which followed soon attracted attention, and towards the end of the 18th century a move was made in Manchester to investigate these outbreaks. Dr. Thomas Percival reported that an epidemic associated with a mill at Radcliffe was due to overwork, poor food, wretched clothing, bad ventilation and overcrowding. In 1802 the government passed an Act for the Preservation of the Health and Morals of Apprentices and others employed in Cotton and Other Mills and Cotton and Other Factories. This was important in that it indicated the right of the Legislature to interfere with conditions in industry, but it had little immediate effect.

The author gives an outline account of the work of the early Inspectors of Factories, especially in relation to children, and of the work of certain outstanding medical men who by their interest and activity put industrial medicine on a sound basis, and continue to develop it. He discusses the hazards associated with ionizing radiation and remarks that we are now at the beginning of a second industrial revolution, when "a gradual linear extension of the previous system will not suffice; we must again become revolutionary in our ideas". He goes on to discuss the inspectorate, the voluntary medical services and other matters, in a stimulating and important address.

II. In the address reviewed above Meiklejohn referred to the outbreak of fever in a cotton mill at Radcliffe, Lancashire, in 1784, which occasioned the request to Thomas Percival and 3 medical colleagues to investigate. He has now reprinted their report, which is otherwise difficult to obtain. It is quite short, and is full of interest, and its emphasis is on ventilation and general cleanliness, and on the danger of overlong working hours, especially for children.

Charles Wilcocks

MURRAY, R. **Quarry Bank Mill. 1. The Story of the Mill.** *Brit. J. Indust. Med.* 1958, Oct., v. 15, No. 4, 293–8, 2 figs. **2. The Medical Service.** *Ibid.*, 1959, Jan., v. 16, No. 1, 61–7, 2 figs. [12 refs.]

The founding of the factory system in England followed almost immediately the invention of the water frame by Richard Arkwright in 1769. Since then no aspect of our social history has attracted more harrowing presentation than the life of the parish apprentices in the dark satanic mills of this period. The records of New Lanark and Deanston in Scotland (FERGUSON, T., *Brit. J. Indust. Med.*, 1948, v. 5, 180) and now of Quarry Bank, England, reveal that there were mill-owners who were deeply concerned for the health and welfare of their workers, young and old.

Quarry Bank Mill was built in 1784 by Samuel Greg. Coincidentally this was the year of the outbreak of epidemic fever at Sir Robert Peel's mill at Radcliffe, which led to the Health and Morals of Apprentices Act, 1802 [MEIKLEJOHN, above]. Greg's mill was situated in the peaceful rural valley of the river Bollin at Styal near Manchester. It contained 3,000 spindles for the spinning of Brazilian cotton and employed 150 men, women and children, the last in the majority. The mill is still working and the original buildings have been maintained in good state. These with the pleasant surrounding fields and woods are now the property of the National Trust. Many of the original documents relating to the business, owners and workers have been preserved. Dr. R. Murray, while working as a medical inspector of factories at Manchester, collected the detailed information presented in this essay. Among the many interesting topics described are the Apprentice House, medical inspection of the workers, pen portraits of the doctors who visited the mill, and medical treatment.

[In the intervening 200 years arising out of these early experiments in the care of the health and welfare of workers, a great system of statutory and voluntary supervision has been developed in factories and mines. All too often, however, we tend to think narrowly in terms of accidents and occupational diseases, and of research and group statistics. Murray in this elegant and scholarly essay makes us feel the warm, throbbing pulse of humanity.] *A. Meiklejohn*

TANT, C. O. & BENNETT, E. O. **The Growth of Aerobic Bacteria in Metal-Cutting Fluids.** *Applied Microbiol.* Baltimore. 1958, Nov., v. 6, No. 6, 388–91.

A variety of bacteria that had been isolated from industrial machine cooling fluids were grown in artificial media, suspended in saline and inoculated into

freshly prepared coolants, held at room temperature. Pseudomonads grew in all products and *Proteus vulgaris* in all but one. The growth of other coliform organisms was variable, depending on strain and coolant. In most cases *Staphylococcus aureus* and *Streptococcus pyogenes* failed to grow, or to survive for more than a few days.

[See also this *Bulletin*, 1957, v. 32, 764.]

R. E. O. Williams

PERRIA, M. Su di una piccola epidemia di cherato-congiuntivite epidemica. [**A Small Outbreak of Epidemic Kerato-Conjunctivitis**] *Igiene Moderna.* 1958, Sept.–Oct., v. 51, Nos. 9/10, 762–9. English summary (7 lines).

The author reports a small outbreak of epidemic kerato-conjunctivitis which occurred in the summer of 1955 at Genoa.

In all 68 cases were detected, including 52 among the clerical staffs of an insurance office and a navigation society, with 16 secondary cases in the families of some of the patients. The outbreak started in mid-July and cases followed at the rate of 1–2 per day until September 9.

Clinically there was conjunctival hyperaemia; hypertrophy of the lower fornix, preauricular lymphadenitis, and nummular keratitis on 3rd–4th day. Both eyes were affected in about 70% of patients. 47 patients recovered completely in 15–30 days without any sequelae, but in the remainder the corneal irritation lasted for nearly 1 year.

Although the insurance society had an eye clinic, the author considers that having regard to the great care taken at the clinic in the sterilization of instruments, etc., the only possible method of infection from one person to another was through the papers, files etc. and even the typewriters and calculating machines passed or used by one clerk after another.

W. K. Dunscombe

BREHM, G. & HOLZMANN, H. Beitrag zur Frage der Spätschäden nach Arbeit mit Pressluftwerkzeugen. [**A Contribution to the Study of Delayed Injury by Pneumatic Tools**] *Berufsdermatosen.* Aulendorf. 1958, Dec., v. 6, No. 6, 309–16, 4 figs. [15 refs.]

The case is described of a man of 47 who in 1958 presented sclerodermatic changes in the palmar aspects of all fingers, shrinkage of the terminal phalanges of both index and little fingers and the middle finger of the right hand associated with attacks of acroasphyxia provoked by exposure to cold. Although the face, the rest of the skin and the cardiovascular system appeared to be normal it was possible to demonstrate some delay in the recovery of normal surface temperature, after chilling, on the distal part of the left upper extremity.

The question had arisen as to how far this man's condition, which interfered with his manipulation of tools and prevented his riding a motor-cycle, could be attributed to military service. He had evidently not himself attributed it to vibration because he did not disclose that he had ever worked with a pneumatic drill until he was asked specifically about it. During his service, however, he had had several severe attacks of tonsillitis one of them associated with arthropathy. The case was not typical of constitutional sclerodermia or of Raynaud's disease [who indeed ever saw one that was!] and yet at least 7 years had elapsed between the employment and the development of any symptoms and the characteristic predilection for the left hand was lacking. In giving their opinion the authors seem to have accepted the possibility that the vibration which, by the way, preceded the tonsillitis, might have combined in some way with the latter to produce the rather equivocal clinical picture that they describe.

J. H. Twiston Davies

JACOBSON, M. G. & HARTZ, N. W. **New Developments in Oxygen Deficiency Testing.** *Amer. Indust. Hyg. Ass. J.* 1959, Feb., v. 20, No. 1, 36–44, 6 figs.

This relates to the atmosphere of mines, manholes, storage tanks, ship's holds etc.

MINISTRY OF POWER. SAFETY IN MINES RESEARCH ESTABLISHMENT. Safety in Mines Research, 1957 [RAMSAY, H. T., Director]. **Thirty-Sixth Annual Report.** 81 pp., 14 figs. & 4 pls. [Numerous refs.] 1958. London: H.M. Stationery Office. [5s.]

This annual report classifies the work of the establishment under 7 headings relating to research and one to testing. It also contains 37 synopses of recent publications by members of the staff and a list of SMRE publications and research reports (Nos. 101 to 158).

Research on explosions and blasting devices included studies of the safeguards needed when firing a delayed sequence of shots to avoid the risk of one of the later charges being exposed, by break-away of rock, and thus igniting firedamp.

A better understanding of pit explosions is urgently needed because 7 involving loss of life occurred during 1957. In 3 cases unsuspected accumulations of gas were responsible and coal dust did not contribute appreciably to the spread. In 2 other cases coal dust played a major part. Research relevant to this problem covers the binding of coal dust, the sampling and analysis of mine-road dusts, properties of stone dust and work in experimental explosion galleries. An experimental mine-road is not available in Britain but information is received from Poland and Western Germany where full-scale trials are carried out. The aerodynamics of dust explosions are concerned with air movements initiated by flame and their reaction upon the flame to determine its speed of propagation. When combustion is confined the unburnt mixture outside the flame zone can be projected as a blast or shock wave; such phenomena have been investigated in a 40 ft. shock tube.

Ignition due to sparks from aluminium and its alloys, and from pyrites has been studied and extra-mural research is in progress on the burning of metallic fragments. The safety of electrical equipment has been under review. A portable instrument for measuring the

concentration of methane is in the prototype stage. Infra-red absorption is used in the laboratory for estimating samples of this gas and also of carbon monoxide.

It had been found that closed circuit breathing apparatus for mines-rescue service was not entirely satisfactory. Improvements have been made with liquid oxygen apparatus and a prototype is under test. The specification of soda lime for absorbing carbon dioxide has been investigated. The delivery of cool, dry air, to the wearer of breathing apparatus remains a problem.

Fires in mines caused no loss of life in 1957 but the risk exists and attention has been given to methods of fireproofing timber and brattice cloth and to the replacement of inflammable hydraulic oils. The foam plug method of fire-fighting is almost ready for practical trial.

Engineering and metallurgical research has been largely connected with winding and haulage gear. It has been established that wrought iron, which wears more rapidly than manganese steel in dry air, performs better than the steel at 60% relative humidity. The loss of strength of chain by wear can now be expressed qualitatively in terms of the decreased diameter of the crown of the link.

Other problems investigated were the embrittlement of iron and steel by strain-ageing and recovery by heat treatment, photo-elastic stress analysis of cage-suspension gear, and the design of roof support equipment.

Examinations of winding and haulage ropes revealed defects due to faulty design of capel, to lack of galvanizing and to migration of the lay. 35% of haulage rope failures are due to corrosion.

Research associated with the pneumoconiosis hazard has involved the taking of many samples by the long-period thermal precipitator to determine number and the Hexhlet to determine mass. On the average, in coal dust clouds, 25 mgm. per cubic metre of respirable dust corresponds to 1,000 particles per cc. between 1 and 5 microns.

The distribution of dust concentration in the neighbourhood of a source has been studied with radio-active gases and nitrous oxide as tracers. Most dust sources are associated with considerable mechanical disturbance of the air which affects the exposure of men working in the vicinity. The movement of a pulse of dust, released by shot-firing, has been simulated and plotted.

A complete analysis of the filter paper stain method of estimating coal dust concentration has led to the conclusion that a handpump indication of less than 330 particles per cc. must be obtained in order to be certain that the true concentration is below 850. Some progress has been made in evaluating the mineral content of coal dust by optical microscopy with transmitted and reflected light simultaneously.

The SMRE has participated in the National Coal Board's Field Research Scheme by determining the mineral content of dust samples by X-ray diffraction. The quartz content of dust in the respirable size range from the first 6 pits ranged from 0·1 to 1·4% on filling shifts and from 2 to 6% on cutting shifts; occasionally, in headings, it rose to 30%. The examination of lung dust from deceased coal workers has continued but the significance of a quartz fraction ranging from 1 to 15% cannot yet be defined.

An excursion into the field of clinical radiology has been attempted by scanning chest radiograms photo-electrically and correlating the frequency-channelled responses with the type of pneumoconiosis.

Research on the mechanism of silicosis has included electron and X-ray studies of the quartz surface, the solubility of etched silicas, and extra-mural animal experiments on the fibrogenic activity of various dusts.

Strata control, the movement of rats in drift mines, and the improvement of an ultra-high-speed camera complete the account of the Establishment's research work.

The Testing Services which it offers are covered in 9 pages relating to explosives, ropes, metallurgical reports, certification of flameproof equipment, haulage vehicles, safety lamps, methanometers, photometers, respirators, helmets and dust control. *C. N. Davies*

ARCH. MALAD. PROFESSIONNELLES. Paris. 1958, Sept.–Oct., v. 19, No. 5, 495–520. **Société de Médecine du Travail de la Région Toulousaine.**

On November 16, 1957, the Society of Industrial Medicine of the Toulouse division of France held a conference at Toulouse on silicosis and allied diseases. 7 papers on various aspects of the subject were presented. These are now published but the discussions, apart from one short item, are not included.

BOLLINELLI, R., BARRÈRE, A. and COSTES, A.
Aspects régionaux de la silicose [*Local aspects of silicosis*]. 494–501.

Until recently the prevalence of silicosis in the Toulouse area was generally regarded as low but this was largely due to the fact that there was no organized means of measuring it. Recent experience shows that the disease is much more common than was thought. The change is due to 3 causes: a heavy incidence of cases among workmen employed in hydro-electric schemes in the Pyrenees, workmen's compensation legislation and better facilities for diagnosis.

Among coal-miners the disease is identified easily and progression is slow. By contrast in the disease in rock workers in tunnelling operations the diagnosis is often long delayed and progression is serious.

Between 1954 and 1957 the Medical Board of 3 doctors investigated 660 cases. These are analysed by nationality, age, occupation and radiological appearances (Cardiff-Douai classification). Attention is directed to 2 groups of cases, so far not subject to compensation: marble cutters at Saint Béat and talc workers at Luzenac.

TAPIE, J. and LE TALLEC, Y.
Le diagnostic différentiel de la silicose [*The differential diagnosis of silicosis*]. 501–504.

There is nothing noteworthy in this paper. It follows the usual pattern citing cases of miliary tuberculosis, sarcoidosis, carcinomatosis and mitral disease.

DARDENNE, P., CASSAGNEAU, J., BOLLINELLI, R., LE TALLEC, Y. and POULET, R.
Le rententissement cardiaque des silicoses pseudo-tumorales [*The cardiac complications of massive silicosis*]. 504–507.

Cardiac complications frequently occur in massive silicosis but true cor pulmonale, in the experience of the authors, is rare. Slight cardiac changes may remain stationary or may even regress, hence the importance of early diagnosis and treatment. On the other hand they may advance owing to aggravation by various factors. Cardiac catheterization is not regarded as a method suitable for routine investigation of cases.

LASSERE, J., BARRÈRE, A., BOLLINELLI, R. and BARRIE, P.
Le problème des silicatoses [*The problem of silicatosis*]. 507–512.

One of the richest deposits of talc occurs in the Ariège district. The mineral contains 51% of silica but none of this is in the free crystalline form (SiO_2). 10 cases of pneumoconiosis were observed among the miners and others employed in handling this material. Radiologically the disease presented nodular and massive shadows. Details of the individual cases are set out in a table.

FABRE, J., PLANQUES, J., TRILLOT, J., SALLES, A. and DUTECH, R.
Le diagnostic anatomique [*Morbid anatomy in diagnosis of silicosis*]. 513–15.

This contribution is a repetition of familiar facts about the morbid appearances of silicosis, coalworkers' pneumoconiosis and associated tuberculosis.

PLANQUES, J., DARDENNE, P. and BARRIE, P.
Déontologie de l'expertise de la silicose par les collèges [*The duties and responsibilities of medical boards in the investigation of silicosis*]. 516–18.

The subject is discussed under 3 main headings in relation to (1) social insurance, (2) the workman, (3) medical colleagues.

Medical boards have a duty to be active in the dissemination of authoritative knowledge of the disease.

JULLIEN, M.
Aspects de la silicose dans une usine d'électro-céramique [*Silicosis in the manufacture of electrical porcelain*]. 519–20.

This is a very brief statement of opinion based on personal observations over a period of 8 years at a factory engaged in the manufacture of small electrical porcelain fittings. The noxious agent is identified as feldspar.

Details of cases are not given but the impression is that they were few in number and so would not justify firm conclusions.

[The transactions of this Conference are almost entirely of interest to local practitioners. The paper on talcosis, however, is important to experts throughout the world.] *A. Meiklejohn*

GRÜMBERG, I. Ist die Silikose eine "Kollagenkrankheit"? **[Is Silicosis a "Collagen Disease"?]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1958, v. 16, No. 5, 592–606. [Numerous refs.]

This article, from the Institute for Hygiene and National Health of the Rumanian Republic in Bucharest, poses the question whether silicosis can be classified as a collagen disease. The author briefly discusses the old definitions which go back almost 70 years, where collagen diseases were supposed to be a group of disorders arising from hitherto unexplained causes, and having in common certain morbid anatomical features, in particular systematic damage to the ground intercellular substance of the fibrous tissue. This damage was later more clearly defined, and today we understand collagen disease to refer to conditions in which there is resolving inflammation, damage to the ground substance, changes in the serum proteins—particularly a rise in gamma globulin—and certain immune reactions. Lastly, and perhaps most important, is the response of these diseases to cortisone therapy. The author states that silicosis is first of all a general disorder of the whole organism, in which the affliction of the lung forms only a part, though this is the most important feature. The disease process proceeds largely in the fibrous tissue of the interstitial parts of the lung. The encounter between dust and tissues usually causes an unspecific inflammation but, unlike other dusts, the inflammation caused by free silicon dioxide is followed by progressive disease, of which the characteristic feature is the nodule of silicosis. The free silica is merely responsible for some aspects of the disorder—the inflammation, and certain fibrotic processes which all occur with any dust damage. However, in the case of silica the crystals also exert a strong influence on the serum and tissue proteins, in which they cause a change. These altered proteins, either alone or in combination with silica crystals, form auto-antigens, and subsequently cause the production of auto-antibodies. The antigen-antibody reactions take place in the fibrous tissue and cause further precipitation of proteins, mucoproteins and lipoproteins.

Thus damage to the ground substance is accompanied or followed by hypertrophy of collagen fibres which eventually give rise to the nodules of silicosis. The actual form of these nodules depends on the presence of dust particles, which give the fibres their particular direction. The existence of an inflammatory process, of immunological reactions, of change in the lability of the serum proteins and of damage to the ground substance, all justify, in the opinion of the author, the classification of silicosis among the collagen diseases.

H. Lehmann

KOBRLE, V. & CHVAPIL, M. Veränderungen von Kollageneiweissstoffen im Verlaufe des Alterns und bei der experimentellen Silikose. **[Changes in the Collagen proteins in the course of Ageing and in Experimental Silicosis]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1958, v. 16, No. 5, 526–38, 2 figs.

There are 2 main types of collagens, insoluble and soluble. The soluble collagens are divided into 3 groups:

(1) The alkali-soluble collagens.
(2) The citrate- or acid-soluble collagens.
(3) The phosphate-soluble collagens, which produce under the electron-microscope a very characteristic picture.

All these 3 collagens have at one time or another been thought to be the precursor of the true insoluble collagen, but recent work suggests that the soluble collagens are actually part of the insoluble collagen, which is not a uniform single protein but is composed of a number of different components.

When the lungs of rats were examined for the different types of collagens, it was seen that with increasing age the soluble types fell and the proportion of insoluble collagens increased. When the rats were treated by intratracheal dusting with silicon dioxide it was seen that within 2 weeks (and more definitely within one month) changes in the composition of the collagens appeared. There was no rise in insoluble collagen, but there was a rise in alkali-soluble collagen.

With progressive disease the concentration of alkali-soluble collagen fell again to normal, but there was a corresponding increase in non-soluble collagen which coincided with the first histological changes in the lungs. *H. Lehmann*

NORVIIT, L. & DI BIASI, W. Bioptische Lymphknotenuntersuchungen nach Daniels bei Silikose. [**Lymph Node Biopsies (Daniels' Method) in Silicosis**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1958, v. 16, No. 5, 503–10, 4 figs. [18 refs.]

This article refers to the work by DANIELS who showed that it is possible to do lymph node biopsies by using the easy access to glands lying in the trigonum omoclaviculare (Daniels, *Brit. J. Dis. Chest*, 1949, v. 16, 360). In 21 miners where there was a suspicion of silicosis, biopsy was performed. X-ray changes in the appearance of the lung were seen in all except one. In 18, silicosis had been suspected either with or without simultaneous tuberculosis, but in none of these had tubercle bacilli been found. In the one case where the X-ray had not shown any changes in the lung picture, the histological findings were negative also. In one other it was possible to confirm the clinical diagnosis of sarcoidosis. In another patient in whom, clinically, carcoidosis and silicosis had been suspected, it was possible to show that the disease was pure silicosis. In another case it was possible to confirm the clinical diagnosis of tuberculosis. A combination of silicosis and tuberculosis has been assumed 9 times. After the examination of the lymph node, it was seen that they included:

1 tuberculosis.
1 tuberculosis plus silicosis.
1 tuberculosis plus suspicion of silicosis.
1 suspicion of silicosis.
2 silicosis alone.
3 times no specific changes were found.

Of eight patients in whom the clinical diagnosis had been pure silicosis, 2 also had tuberculosis.

The conclusion is reached that the lymph node biopsies would form a valuable investigation in diagnosis of lung disease, particularly when the suspicion of silicosis is entertained. *H. Lehmann*

GROSS, P. **The Perivascular Spaces in the Lung.** *Arch. Pathology.* 1958, Nov., v. 66, No. 5, 605–9, 6 figs.

From studies of many tissue sections of animals' lungs the author suspected that the perivascular spaces seen around the pulmonary vessels were in the main not true lymphatic spaces as has been assumed hitherto. Rats and guineapigs were given quartz dust by inhalation and intratracheal injection and were killed at various intervals. The lungs of these animals were compared with those of rats and guineapigs raised under germ-free conditions. The author was able to distinguish between spaces formed by splitting of peri-adventitial fibres of the vessels and true lymph spaces which had a definite endothelial lining. Perivascular spaces were very common in the animals given quartz and were most likely caused by oedema but such spaces were rarely seen in the control animals. *D. Rivers*

GROSS, P., WESTRICK, Marian L. & MCNERNEY, J. M. **Experimental Silicosis. The Morphogenesis of the Silicotic Nodule.** *Arch. Indust. Health.* Chicago. 1958, Nov., v. 18, No. 5, 374–88, 15 figs. [13 refs.]

Quartz dust was administered to rats by inhalation and intratracheal injection and animals were killed at intervals of 1, 2, 3 and 4 months. Guineapigs and rats raised in "germ-free" conditions were used as controls. Guineapigs subjected to inhalation of china clay dust for one year were injected intratracheally with an avirulent human tubercle bacillus (R1Rv strain) and were included for comparative purposes. The lungs of the animals which had received quartz by inhalation showed silicotic nodules arising from the alveolar walls which abut on vessels and not in the spaces between vascular adventitia and alveolar walls. The nodules in the lungs of rats which had received quartz dust by intratracheal injection were predominantly intra-alveolar and remote from vessels. The authors believe that their observations contradict established views on the pathogenesis of silicosis and maintain that silica particles penetrate into interstitial tissue of the lung without the aid of phagocytes. [Their histological evidence on the site of development of silicotic nodule is convincing but is inadequate to support their contention that silica particles pass into interstitial tissue in a free state without phagocytosis.] *D. Rivers*

LÖBLICH, H. J., KOCH, W., SOFFGE, K. H. & NORDMANN, M. Die Resorption einverleibten Staubes. Feinkörnige Stäube (Kalkspat, Spateisenstein, Talk, Rutil). [**The Absorption of Deposited Dust. Fine Dusts (Calcite, Siderite, Talc and Rutile)**] *Beiträge z. Silikose-Forschung.* 1957, No. 50, 1–10.

Suspensions of the dusts were prepared in serum and in Tyrode solution (with ultrasonic dispersion) containing about 1 mgm. in 50 cc. They were injected through a cut into the mesentery of rabbits and the deposit

of dust in the tissue was examined microscopically *in vivo* at intervals up to 10 days after injection. The tissue film examined was about 50 microns thick. The field was viewed with crossed polarizers so that doubly refracting particles would show up as bright points of light against a dark field. It was found that quartz dust was only visible in sizes exceeding 3 microns because its double refraction is slight and the indices of quartz and tissue are quite close. Other materials, more favourable optically, were therefore tried.

Calcite particles dissolved and disappeared and siderite, possibly owing to its transformation into the soluble ferrous bicarbonate, also vanished. Talc seemed a promising material but the experiment was unsuccessful.

Rutile, which is highly doubly refracting, was visible down to 0·5 micron. The positions of the crystals in the deposit formed after injection remained unchanged for 10 days. Deposits of fibrin were seen near the particles but it was not known whether the particles tended to lodge in the fibrin fibres or whether the fibres formed near the crystals. Certainly no migration of the dust to the lymphatic vessels was seen and no appreciable phagocyte activity was noted.

C. N. Davies

SAUER, F., LAUGHLAND, D. H. & DAVIDSON, W. M. **Silica Metabolism in Guinea Pigs.** *Canadian J. Biochem. & Physiol.* 1959, Feb., v. 37, No. 2, 183–91. [18 refs.]

"The excretion of silica $(SiO_2)_n$ in urine and feces was determined following the oral and intraperitoneal administration of silica to guinea pigs. The urinary excretion of silica after oral administration generally reached a maximum value that was not exceeded by increasing the dose. The urinary excretion after intraperitoneal administration was considerably greater than after oral administration. The results of these experiments suggested that orally and intraperitoneally administered silica is depolymerized to the soluble form prior to excretion in the urine."

VELICAN, C., LATIS, G., POPA, M., POPA, G. & STEINBACH, M. **Investigations concerning the Pre-Radiological Stage of Silicosis.** *Brit. J. Indust. Med.* 1959, Jan., v. 16, No. 1, 40–42.

This team of research workers, working in the Therapeutics Institute of the R.P.R. Academy, Bucharest, studied the biochemical changes in the blood, sputum and urine in a group of workmen, newly engaged for work at a gold mine.

The ore was a gold-bearing quartz, which contained free and combined silica amounting to 72%. Dust exposures underground varied, according to occupation, between 150 and 45,000 particles per cc. of which 50–68% were between 1 and 3μ in diameter. One case of radiological silicosis had been observed after 3 years' employment but more usually radiological changes did not occur until after 5 to 7 years.

The following investigations and determinations were made at 6-month intervals for 2 years: physical examination, chest films and radioscopy, electrocardiogram, basal metabolism, differential blood count and haematocrit, erythrocyte sedimentation rate, blood silica (King's method), blood potassium (Hoffman and Jacobs' method), blood calcium (Clark-Collip's method), ascorbic acid in the blood (Roc and Knether's method), blood cholesterol (Sackett's method), proteinaemia (Hinsberg-Lang's method), silica in the sputum (King's method), and urine analysis.

The investigation comprised 33 workmen, aged 18 to 30 years: 22 underground and 11 surface workers. None had previously been employed in a silicosis hazard. Only those in whom the above examinations were normal were followed up. Exposure to dust varied widely from a maximum of 45,000 particles per cc. at the rock face to no dust in surface clerical work. In the group of 6 miners—the most heavily exposed workmen—the authors observed a statistically significant rise of blood silica and of the eosinophil and monocyte counts. They also noted a significant fall in the red cell count.

Differences in the value of other biological indices were not statistically significant in this group, nor were there any significant differences in the other groups exposed to less dust.

The authors submit that the humoral phase of silicosis begins during the second year of exposure to dust, and precedes by 3 to 7 years the characteristic radiological changes.

[This contribution would have been improved by a table presenting the data of the individual 6 cases, instead of averaging them for the group as in tables 1 and 2. The statement that the 22 underground workers were divided into 4 groups, should read 3 groups, namely, A, B and C.

The subject-matter of this article was previously published elsewhere—this *Bulletin*, 1958, v. 33, 1050.]

A. Meiklejohn

KO, YUAN-CHING. **Vital Capacity and Chest Volume Index among Gold-Miners in Formosa.** *J. Formosan Med. Ass.* 1958, Aug. 28, v. 57, No. 8, 516–23.

In this competent study a new index of lung elasticity, the vital-capacity-chest-volume index (VCI) was determined on 273 workers in a Formosan gold mine of whom 47 had worked only as drillers, 113 entirely at jobs other than drilling and the remainder (given in error as 133 instead of 113) in both categories.

The index, which is vital capacity divided by length × width × thickness of the chest, was compared with Roentgeno-fluorography examinations.

Mean VCI fell progressively from normal through silicosis 1st, 2nd and 3rd stage, each step being significant. Tuberculosis co-existing with silicosis had a variable effect on the index.

A highly significant difference was found between mine workers and surface workers in the rate of fall of VCI with age: the mine workers' index fell more rapidly, especially those engaged in drilling.

[The value of this index would to some extent depend on uniformity of lean mass to total body weight.]

M. L. Thomson

HASSELT: INSTITUT D'HYGIÈNE DES MINES. Communication No. 150. L'hémodynamique dans les pneumoconioses. Premiers résultats [**Blood Circulation in Pneumoconiosis; First Results**] [KREMER, R. & BRASSEUR, L.]. 1958, Jan. 15, v. 13, No. 1, 20 mimeographed pp., 2 figs. [25 refs.]

CHIVERS, C. P. **Respiratory Function and Disease among Workers in Alkaline Dusts.** *Brit. J. Indust. Med.* 1959, Jan., v. 16, No. 1, 51–60, 2 figs. [20 refs.]

A large alkali industry is carried on in mid-Cheshire, England. Production is distributed over 4 factories. At works A caustic soda and its by-products and at works B and C sodium carbonate and its by-products are manufactured. These works employ respectively 2,500, 1,000 and 700 workers. The processes are dusty but only a small proportion of the workmen are continually exposed to heavy concentrations of dust. The alkalinity of the different dusts is in the range of *p*H 8·5 to 12·5. Works D, employing 200 workmen, is situated in the open country and produces brine from boreholes in the earth. In this works there is no dust.

In 1954, after an investigation in this group of alkali workers, ARCHIBALD [this *Bulletin*, 1954, v. 29, 635] reported the occurrence of inflammation of the nasal mucous membrane accompanied in some cases by perforation of the nasal septum. During the years 1954 to 1956 Chivers studied the effects of the inhalation of the alkaline dusts on the lungs among 337 male volunteers from factories A, B and C; 126 workmen from factory D constituted the control group.

The study included the industrial history, measurement of pulmonary ventilation by means of a simple spirometer with a constant speed kymograph, sickness absence and smoking habits. Chest radiographs on miniature film were made in 20 workers with long service and exposure to dust. No pneumoconiosis was detected. A reduction of respiratory efficiency was observed but the author concluded that in the production of this smoking habits played a more important part than the alkaline dusts. *A. Meiklejohn*

DOWLING, T., DAVIS, R. B., CHARSHA, R. C. & LINCH, A. L. **Lead-in-Air Analyzer. A Specialized Air Sampling and Analysis Kit.** *Amer. Indust. Hyg. Ass. J.* 1958, Aug., v. 19, No. 4, 330–37, 7 figs. & 4 charts.

The manufacture and handling of motor fuel anti-knock compounds containing tetra-ethyl lead are processes in which rigid environmental control is especially necessary if hazards to health are to be avoided. This paper describes a portable "Lead-in-Air Analyzer" which incorporates apparatus both for air sampling and air analysis. The former consists of a power assembly, aspirator, charcol trap and scrubber, and includes a thermometer, calibration chart and timer. The analysis apparatus consists of 2 comparator tubes, a Hellige Comparator, a Deeminac Water Purifier and 8 boxes of reagents. A Deeminac water purifier provides the equivalent of pure water. The filter holds the ionized impurities and thus eliminates minerals and salts including chlorides. Each box of reagents contains sealed vials loaded with the exact amount of lead-free chemicals required for one determination. These chemicals are:—

Quantity	*Description*	
10 ml.	0·5 normal iodine	(A lead-free water solution of iodine and potassium iodide)
15 ml.	Solution A	(A lead-free water solution of potassium cyanide, sodium sulphite, ammonium citrate and ammonium hydroxide)
0·2 mgm.	Dithizone	(Diphenylthiocarbazone)
5 ml.	Chloroform	

The air sampling unit is an adaptation of a special high efficiency micro-aspirator [CHARSHA & LINCH, this *Bulletin*, 1957, v. 32, 1076] powered by a Freon-12 propellent. The modifications included a reduction of the air sample from 4 to 2 cubic feet and the replacement of the special scrubber described by SNYDER *et al.* [*ibid.*, 1948, v. 23, 866] with a midget impinger manufactured to rigid specifications, including close dimensional tolerances. In the tetra-ethyl lead industry a major requirement for a field unit is that it shall not be capable of igniting flammable or explosive vapours. No response was obtained when this insulated sampling unit was tested for "'static' generation".

Interested readers should consult the original for full details concerning the apparatus and how to operate it and carry out the chemical analyses. Calibration tests were carried out on the unit and the results are given in a number of charts.

P. J. R. Challen

HICKLING, S. **Vanadium Poisoning.** *New Zealand Med. J.* 1958, Dec., v. 57, 322, 607–8.

This short paper contains a report of a probable case of vanadium poisoning in a man engaged in cleaning out the boiler of a small oil burning ship. A great deal of dust is produced in this process but the man had decided to carry on with the work without a respirator as stocks of respirator pads had run out. Within 2 hours of beginning his work he had symptoms of severe coryza and headache for which he attended the Wellington Industrial Health Clinic. He was taken off work and the symptoms disappeared in a day or two. When first seen his tongue had a dense black coating with a greenish tinge but in a few days the colour turned deep green and then yellowish green before disappearing.

Samples of soot collected from the boilers were analysed and the ash was found to contain 20% of vanadium. The fuel oil used in these boilers which is of Middle Eastern origin is quoted in the literature as containing an average of 16% of vanadium.

M. E. Delafield

HILL, W. H., MERRILL, Jean M., LARSEN, R. H., HILL D. L. & HEACOCK, J. F. **Colorimetric Determination of Boron Hydrides by means by Phosphomolybdic Acid.** *Amer. Indust. Hyg. Ass. J.* 1959, Feb., v. 20, No. 1, 5–12, 5 figs. [11 refs.]

CAMPBELL, E. E., MILLIGAN, M. F. & LINDSEY, Jean A. **The Determination of Thallium in Urine and Air.** *Amer. Indust. Hyg. Ass. J.* 1959, Feb., v. 20, No. 1, 23–5, 2 figs.

SUNDERMAN, F. W., WEST, B. & KINCAID, J. F. **A Toxicity Study of Iron Pentacarbonyl.** *Arch. Indust. Health.* Chicago. 1959, Jan., v. 19, No. 1, 11–13. [10 refs.]

An amber liquid of high toxicity, $Fe(CO)_5$ needs care in storage and during laboratory work. On heating it yields iron and carbon monoxide. "It may be decomposed on exposure to air and ignites spontaneously," Its vapours form explosive mixtures with air. On exposure to light it may be slowly decomposed to give $Fe_2(CO)_9$ and CO.

Acute inhalation toxicity experiments were carried out in mice and rats, exposed for 30 min. to the vapour of iron pentacarbonyl, which had been dissolved in ethyl ether, in concentrations varying from 3·62 to 1·57 mgm. per litre, and from 1·88 to 0·66 mgm. per litre, respectively, in order to determine the 3- and 5-day mortality ratios. The LD50 values for a 30 min. exposure were estimated to be 2·19 mgm. per litre for mice and 0·91 mgm. per litre for rats. In contrast nickel carbonyl is more toxic for mice than for rats.

To discover whether any antidote is effective, mice after being exposed for 30 min. to 3·0 mgm. per litre, were divided into groups of 10. The 3- and 5-day mortality ratios were compared in 5 groups receiving no treatment with those in 10 groups receiving one of the following parenterally: Dimercaprol (BAL), 7·5 or 5·0 mgm./kgm., divided into 4-hour doses; dl-penicillamine, 100 mgm./kgm.; sodium diethyldithiocarbamate (Dithiocarb), 100 or 50 mgm./kgm.; and edathamil calcium-disodium in total doses of 100, 300, 350 or 1,000 mgm./kgm., all except the first in divided doses. None of these measures was effective except edathamil, 100 mgm./kgm., which gave some protection, with mortality ratios of 3/10 and 4/10, though with the larger doses the ratios were higher; one-half survived on an immediate dose of 250 followed 4 hours later by 100 mgm./kgm. These results are in contrast with those obtained in nickel carbonyl poisoning.

M. Patricia Fitzsimons

BROWNING, Ethel. **Toxic Solvents: a Review.** *Brit. J. Indust. Med.* 1959, Jan., v. 16, No. 1, 23–39. [Numerous refs.]

This important review by the author of the Medical Research Council's famous report, *The Toxicity of Industrial Organic Solvents* [this *Bulletin*, 1953, v. 28, 834], should be read in the original. It is in effect an addendum to the last edition, comprising numerous critical abstracts of the growing literature on old and new chemical compounds, with an extensive and valuable bibliography. Many individual solvents are reviewed. In addition the author notes developments in experimental physiology of methods of assessing acute and chronic toxicity, and their relationships and differences. Knowledge of the metabolism and detoxification of solvents has been facilitated by spectrophotometric methods, paper chromatography and radio-active tracers. Methods outlined for estimations of atmospheric concentrations of mixed contaminants include colorimetric analyses, catalysed combustion, vapour pressure method, absorption spectrophotometry and gas chromatography.

Among several outstanding developments the author concludes that 3 features are noteworthy: the ever-growing ability to forecast by animal experiment not only whether a solvent is likely to be toxic to human beings but also the nature and site of the toxic effect; modern metabolic investigations, on exposed human beings as well as animals, shedding light on why one toxic solvent attacks particular organs and tissues while another of the same chemical group does not, thus opening up the possibility of replacing extremely toxic substances by safer ones; and the annual publication of those values of atmospheric concentrations based on research and experience below which persons at work can be expected to suffer no significant or permanent injury to health. New solvents, investigated by modern methods, have on the whole proved less hazardous, particularly from the viewpoint of chronic systemic poisoning, than some of the older ones whose toxicity was revealed by involuntary human experiment.

M. Patricia Fitzsimons

SHIELS, D. O. **Poisoning due to Use of Carbon Tetrachloride.** *Med. J. Australia.* 1958, Nov. 29, v. 2, No. 22, 729–31.

From the Industrial Hygiene Division, Department of Health, Victoria, 10 years after the event, comes this account of 15 men affected to varying degrees by the vapour of carbon tetrachloride and also probably by phosgene. They were working in or near a small unventilated evaporator room in a cargo ship. In this room 6 men cleaned out the coils with carbon tetrachloride, later calculated to have been 30,000 p.p.m., and 4 plumbers used oxy-acetylene burners for a short time till forced to stop because of the fumes. Several men had hepato-renal injury and one, the chief refrigeration engineer, died on the 9th day with toxic changes in kidneys, liver, trachea and lungs. Early in the illness 10 men had shortness of breath and cough; 8 of them had smoked during work. It was likely that these symptoms were caused by phosgene formed by the action of the oxy-acetylene flame or the heated cigarette ends, or both, on the carbon tetrachloride vapour. Treatment of 3 patients with methionine tablets caused a rapid improvement in their condition after unsuccessful treatment for 6 weeks by conventional methods. Early symptoms included those of liver damage and kidney involvement and indicated damage to the respiratory tract, but there was no consistent relationship between the severity of the initial symptoms and the presence or absence of abnormalities in the liver function tests, blood and urine examinations and chest X-ray examinations performed 12 to 14 days after exposure. 3 case histories and tables giving results illustrated this.

These cases are of interest because of the respiratory symptoms and because they apparently confirm the value of methionine for the treatment of liver damage caused by toxic chlorine compounds. [Meanwhile E. BROWNING in a new edition of the Medical Research Council Reports *Toxicity of Industrial Organic Solvents* (this *Bulletin*, 1953, v. 28, 834) points out that methionine therapy has proved of debatable value in the treatment of poisoning of human beings by carbon tetrachloride, and in *Brit. J. Indust. Med.*, 1959, v. 16, 23 (above), reports that in fatal cases of carbon tetrachloride poisoning the damage to internal organs is usually most marked in the liver; in other cases the kidneys are more severely affected and in all cases there is some lung involvement. See too this *Bulletin*, 1959, v. 34, 62, for a clinical analysis of patients with anuria from carbon tetrachloride poisoning; death was thought in most cases to be due to hepatic insufficiency.]

M. Patricia Fitzsimons

TORKELSON, T. R., OYEN, F., MCCOLLISTER, D. D. & ROWE, V. K. **Toxicity of 1,1,1-Trichloroethane as determined on Laboratory Animals and Human Subjects.** *Amer. Indust. Hyg. Ass. J.* 1958, Oct., v. 19, No. 5, 353–62, 2 figs. [24 refs.]

1,1,1-trichloroethane (methyl chloroform) (chlorothene) has become widely used as a solvent in the last few years, particularly in cold degreasing operations. There has been some confusion in the literature as to the toxicity of this isomer.

This article reports the effects of the liquid upon skin and eyes of rabbits and of intragastric administration of single doses to various species and of repeated inhalation of vapour by various species. Laboratory and field experience with human subjects is also described.

One application to the eyes of rabbits resulted in some pain and inflammation which subsided quickly without corneal damage. Direct application of the liquid to the shaven skin indicated that the material was of low toxicity by this route. The skin at the site of application showed only slight reversible irritation. Oral toxicity was also low.

Repeated inhalation of vapour (500 p.p.m. for 7 hours a day for 5 days a week for 6 months) resulted in no adverse effects compared to the controls in male and female rats, guineapigs, rabbits and in 2 female monkeys. With exposure to very much higher concentrations of vapour (10,000 p.p.m. for 5 days a week for 3 months for periods varying from 3 minutes to 1 hour per day) the only evidence of organic injury in male rats was a barely significant increase in liver weight in those exposed for 1 hour a day. This concentration also caused various degrees of anaesthesia. Guineapigs exhibited more susceptibility to high concentrations than rats. Appearance and growth and organ weights remained normal but there was some irritation of the lungs and fatty changes in the liver.

The data obtained on human subjects were in agreement with those obtained from the animal experiments. No evidence of injury was found from exposures of 500 p.p.m. for 7 hours to 1,900 p.p.m. for 5 minutes. Exposure to 900–1,000 p.p.m. for 1 hour resulted in slight incoordination and some loss of equilibrium.

Conclusions are that when handling this solvent it is advisable to protect the eyes from splashes and if clothing becomes soaked in the liquid by accident it should be promptly removed. Concentrations of vapour in a workroom should be maintained below 500 p.p.m. —exposure to 1,000 p.p.m. on any occasion should be limited to a few minutes.

2 cases in which individuals have died after exposure have been reported—in each instance the concentration was very high in unventilated tanks. (Epinephrine should never be given to anyone overcome with a chlorinated hydrocarbon because of the risk of inducing ventricular fibrillation.) *T. O. Garland*

BARDODĚJ, Z. & KRIVUCOVÁ, Marie. Hodnota a použití exposičních testů (V). Stanovení trichlorethylalkoholu (kyseliny urochloralové) jako exposiční test u pracujících s trichlorethylenem. [**The Value and Use of Exposure Test V. Determination of Trichlorethyl Alcohol (Urochloralic Acids) as an Exposure Test on Workers with Trichlorethylene**] *Ceskoslov. Hyg.* Prague. 1958, v. 3, No. 5, 268–72, 5 graphs. [15 refs.] English summary.

The authors have investigated the method of KUBIS and LISKOVÁ (*Bratislav. lek. Listy*, 1956, v. 36, 153) for determining urochloralic acid (trichlorethanol vapour glucuronide) in the urine as an index of exposure to trichlorethylene vapour in industrial workers. The method is based on the oxidation of urochloralic acid with chromic acid to trichloracetic acid, which is determined by a colour reaction with alkali and pyridine. The average ratio of urochloralic acid to trichloracetic acid in the urine of persons breathing trichlorethylene in the maximum permissible concentration of 0·4 mgm. per litre was 2 : 1. With a maximum permissible limit of trichloracetic acid in the urine of 160 mgm. per litre the limit for trichlorethanol would therefore be 320 mgm. per litre, or 700 mgm. per litre conjugated as urochloralic acid. *D. J. Bauer*

PANG, H. C., HASHIMOTO, T. & MURAKAMI, H. [**The Effect of Glutathione on CO-Poisoning**] *Japanese J. Nation's Health.* 1958, Dec., v. 27, No. 4, 246–9, 3 figs. [In Japanese.]

The English summary appended to the paper is as follows:—

"Because glutathione (GSH) had demonstrated remarkable effects on the recovery of CO-poisoned workers at a gas-producing factory, the authors carried out some experiments on the relation between CO-poisoning and GSH.

"The following conclusions were obtained:

"1) The administration of GSH had no effect on the dissociation of COHb. (Fig. 1)

"2) GSH concentration in the blood of CO-poisoned rabbits showed the tendency of decrease. (Table 1)

"3) In the case of CO-poisoned mice it was noticed that the depression of tissue respiration could be recovered to a normal level by the administration of GSH. (Fig. 2)

"The recovery might be attributed to the GSH action of retaining the respiratory enzyme in the thiol form."

GAGE, J. C. **The Toxicity of Epichlorhydrin Vapour.** *Brit. J. Indust. Med.* 1959, Jan. v. 16, No. 1, 11–14, 3 figs.

Versatile apparatus for exposing animals to predetermined concentrations of toxic substances in air, evolved in the Industrial Hygiene Research Laboratories of Imperial Chemical Industries, described in detail and in diagrams, permits visibility through Perspex walls and prevents atmospheric contamination. The method also permits known and varied concentrations to be generated without knowledge of the physical constants of the substance; impure samples or mixtures can be examined without progressive change in the exposure chamber atmosphere; the substance is volatilized without heat and the bulk is not exposed to continuous aeration with possibility of chemical changes; with a solution of a non-volatile liquid or solid in an inert volatile solvent a fine mist or dust is produced, and low dilutions of a gas can be directly injected.

The epichlorhydrin atmospheres were prepared by atomizing solutions into a metered stream of air by means of a controlled fluid-feed atomizer fused to a glass syringe driven by a slow injection apparatus modified for vertical drive at different speeds. In each exposure chamber 8 rats, on a stainless steel wire grid, were separated from each other by partitions radiating from the central glass channel, with a second grid above the partitions to prevent them climbing over. Epichlorhydrin vapour concentrations, for 6 hours a day on 5 days a week, varied from 120 p.p.m. for 11 exposures to 56, 27, 17 and 9 p.p.m. for 18. At 120 p.p.m. after 3 hours the rats showed laboured breathing and later lethargy, nasal discharge, loss of weight, leucocytosis and increased urinary protein excretion; one died after 11 exposures. All showed lung oedema and consolidation, atrophy of renal cortical tubules and hepatic congestion. At 56 p.p.m. they only showed lethargy, respiratory distress and nasal discharge, with no pathological changes. In rats and also in rabbits nasal irritation did not appear at 9 p.p.m., the animals remaining healthy after 18 and 20 exposures respectively. A maximal allowable concentration of 5 p.p.m. epichlorhydrin is recommended.

M. Patricia Fitzsimons

LEACH, L. J., SPIEGL, C. J., WILSON, R. H., SYLVESTER, G. E. & LAUTERBACH, K. E. **A Multiple Chamber Exposure Unit designed for Chronic Inhalation Studies.** *Amer. Indust. Hyg. Ass. J.* 1959, Feb., v. 20, No. 1, 13–22, 5 figs. & 6 diagrams.

FEINSILVER, L., PERREGRINO, J. A. & SMITH, C. J., Jr. **Estimation of Hydrazine and Three of its Methyl Derivatives.** *Amer. Indust. Hyg. Ass. J.* 1959, Feb., v. 20, No. 1, 26–31, 2 figs.

BOLTON, N. E., JOHNSON, J. B., MCDERMOTT, W. H. & STACK, V. T., Jr. **Determination of Tributylphosphine in Air.** *Amer. Indust. Hyg. Ass. J.* 1959, Feb., v. 20, No. 1, 32–5, 6 figs.

JACOBSON, K. H., CHRISTENSEN, M. K., DEARMON, I. A., Jr. & OBERST, F. W. **Studies of Chronic Exposures of Dogs to GB (Isopropyl Methylphosphonofluoridate) Vapor.** *Arch. Indust. Health.* Chicago. 1959, Jan., v. 19, No. 1, 5–10, 1 fig.

GB, known as Sarin, a toxic "nerve gas" which inactivates cholinesterase, is at ordinary temperatures a liquid with an appreciable vapour pressure. 4 groups of 3 dogs (7–20, 7–4, 5–20 and 5–4) were exposed in a dynamic gassing chamber for 6 months to GB vapour at a daily Ct of 10 mgm. min./m.^{3} [Ct indicates concentration related to time.] Exposure times were sometimes varied in order to compensate for Ct variation due to variations in concentration. The appropriately numbered groups were exposed for 7 or 5 days per week, in order to study week-end recovery, and for 20 minutes or 4 hours daily.

All had miosis and cholinesterase inactivation but no significant changes in weight, electrocardiograms, blood counts or temperatures, except one in the 7–20 group which died of accidental heat stress after 5 months; there was occasional salivation, rhinorrhoea and dyspnoea. In those from each group killed shortly after the experiment there was thickening of the musculature of the bronchioles and alveolar ducts, probably caused by chronic constriction; dilatation of the bronchial glands, with some flattening of the epithelium; no significant depression of brain cholinesterase activity, except in a 7–20 dog, the most severely poisoned group.

The blood cholinesterase activities dropped rapidly at first and then remained almost constant, the individual values ranging from 12% to 30% of normal. Exposure for 7 days a week caused severer effects than for 5 days at the same daily Ct; exposure for 20 minutes a day (GB concentration, 0·5 mgm./m.^{3} or 0·09 p.p.m.) caused severer effects than exposure to the same Ct for 4 hours a day (GB concentration, 0·04 mgm./m.^{3} or 0·007 p.p.m.), The reason for the latter is possibly that the organism was better able to deal with a given amount of poison when the exposure time was long. Though the dogs became adjusted after several weeks and seemed to improve slightly, their condition later regressed and they appeared not likely to survive stress.

After removal from exposure the blood cholinesterase started to regenerate at a rate of about 1% per day from activity levels of about 30% of normal. One dog each from groups 5–4, 7–4 and 5–20 was permitted to recover from the exposure. They recovered rapidly, sired successful litters and several months later were found normal.

The apparent correlation between cholinesterase inactivation and the frequency and severity of other toxic signs suggests blood cholinesterase inactivation as an objective criterion of chronic poisoning.

M. Patricia Fitzsimons

MÉNDEZ-CASHION, Dolores, CÁCERES DE COSTAS, Margarita, NAZARIO, R. & ORTIZ, A. **Poisoning by Organic Phosphorous Insecticides.** *Bol. Asoc. Med. de Puerto Rico.* 1958, Aug., v. 50, No. 8, 277–89, 1 fig.

Attention is drawn in this paper to the danger of organic phosphorus insecticides to children in the home.

The authors have recently had experience of 7 children in San Juan, Puerto Rico, who were poisoned at home by 1 of these insecticides, apparently parathion, which was being peddled in unlabelled envelopes. The first case was in a girl aged 2 years who had been playing under a bed where the insecticide mixed with cooked rice had been sprinkled. The signs and symptoms and the course of the poisoning, which ended in recovery, are described. There are 4 tables which set out the particulars of all 7 patients and the evidence of ingestion of parathion, the symptoms and signs, the findings ot laboratory examination of urine and blood and of the treatment given. 2 children died.

In the discussion on diagnosis and its difficulties in the absence of a clear history of ingestion of an insecticide mention is made of the fact that parathion, which was probably responsible for these 7 poisonings, is marketed under at least 20 trade names. A list of these names is given.

Thiophos	Niran
Aphamite	Genithion
Mackothion	Alkron
Corothion	Kilphos
Paradust	Paraphos
Penphos	Phos-Kill
Vapo-Phos	Planthion
Compound 3422	DNTP
AAT	DPP
E-605	

Treatment is discussed and in these cases it consisted of maintenance of respiration, atropine in larger doses than is usually employed, gastric lavage, cleansing the skin where indicated and supportive measures. Stress is laid on the importance of making parents aware of the increasing hazard of poisoning in children by household substances and the need for urgency in obtaining medical attention. *M. E. Delafield*

Bourret, J., Tolot, F., Pollet, M. L. & Genevois, M. Les dermatoses professionnelles provoquées par le formol et ses dérivés industriels. [**Occupational Dermatoses Produced by Formaldehyde and its Industrial Derivatives**] *Arch. Malad. Professionnelles.* Paris. 1958, Nov.–Dec., v. 19, No. 6, 611–15.

Attention is drawn to the extensive industrial use of formaldehyde in the processing of plastics, glues, leather, rubber and crease-resisting textiles. A useful clinical description is based on the detailed observation of 13 cases of dermatitis. French law which works on a system of limiting indexes does not at present envisage compensation for the results of allergy to formol; and it is therefore urged that there is a strong case for adding this allergen, for so long notorious in the pathological laboratory, to the schedule.

J. H. Twiston Davies

Huriez, C. Les tests cutanés dans les sensibilisations professionnelles. [**Cutaneous Tests in Industrial Allergy**] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1958, Dec., v. 6, No. 8, 888–99.

The author, having evidently given the matter of industrial dermatitis some anxious thought, clearly believes that all would be well—provided of course that the law could be changed so as to make his activities really worth while—if only a specialized organization could be set up to deal with this malady, which he estimates to involve 1% of the whole working population.

Those dermatologists who still think in naive materialistic terms of occupational dermatitis would certainly endorse his views and welcome the adoption of his plan for its own sake, and the appetite of others for more knowledge of this puzzling sign of the times is stimulated by the proposal. *J. H. Twiston Davies*

Cember, H., Watson, J. A. & Spritzer, A. A. **Bronchogenic Carcinoma from Radioactive Cerium Fluoride.** *Arch. Indust. Health.* Chicago. 1959, Jan., v. 19, No. 1, 14–23, 9 figs. [14 refs.]

Experiments with intrapulmonary $^{144}CeF_3$, diffusely distributed throughout the lungs to simulate inhalation, produced neoplasms in rats, and indicate that the maximal permissible concentration is set too high. ^{144}Cerium is a beta-gamma emitter with a half-life of 275 days; the decay product ^{144}Pr, also radio-active, has a half-life of 17·5 minutes. Suspensions of 30 μgm. CeF_3 particulates, which contained specific varied amounts of $^{144}CeF_3$, were injected intratracheally in anaesthetized rats. 4 groups received the radio-active cerium in doses of 5, 15, 25 or 50 μc. per rat, giving an absorbed dose in rads of 2,400, 5,100, 10,700 or 21,000 respectively, and autoradiographs of lung sections illustrate good distribution. A control group of 29 received the non-radio-active CeF_3 only; 20 served as colony controls.

An acute radiation effect occurred in the 3 highest-dosed groups; the LD50 30-day dose was 45 μc. Pneumonia was the cause of death, with haemorrhagic consolidation and also exudate in the bronchial system, pleura and pericardium. Bronchogenic carcinoma occurred in all 4 experimental groups, the frequency, according to ascending dosage, being 1/27, 1/23, 7/28 and 4/15. In addition to these 13 squamous-cell carcinomata, there were among these 93 animals 14 cases of bronchial squamous metaplasia; among 49 controls there was one. The carcinoma in the 15 μc. group was found after death 48 days after exposure. An early carcinoma was found in a rat killed 178 days after exposure to 5 μc. Of the 15 rats receiving 50 μc., 9 had died within 50 days of exposure, and the 4 with well differentiated tumours were among the 6 survivors, 3 dying between 83 and 86 days after exposure and the fourth after 228 days. No metastases were observed. Squamous-cell carcinoma is not known to occur spontaneously in the lungs of rats.

M. Patricia Fitzsimons

Buckland, C. W., Jr. **Interpretation of Regulations governing the Shipment of Radioactive Material.** *Arch. Indust. Health.* Chicago. 1959, Jan., v. 19, No. 1, 33–43, 7 figs.

As the author states "The number of radio-active shipments originating from the Los Alamos Scientific Laboratory [N. Mex.] has increased to the point where

interpretations [reviewer's italics] of the existing regulations have had to be made available in a concise and systematic form for the average monitor".

The word "monitor" signifies the person responsible for despatch or acceptance of radio-active supplies. He has to be conversant not only with the general nature of the supplies handled but with the extent to which any emitter radiation is going to prove acceptable to the authorities; these general limits are specified on H. A. Campbell's Tariff No. 10, issued on May 18, 1957. In general it may be said that any package giving evidence of external alpha or beta radiation is condemned, for it is almost certainly due to contamination whereas some gamma radiation is allowed; it is impossible or impracticable to stop all gamma rays within an average sized container holding moderate radio-active quantities.

The whole of the present regulations for the U.S.A. are explained for the benefit of the monitors. Others will be impressed by this present day attempt to limit the exposure of people to unwanted radiation. Reference is made to the work of the Isotope Division of the A.E.R.E. Harwell, England. *S. Russ*

Sanitation

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

KRAUS, P. Ein handliches, hydromechanisches Probeentnahmegerät zur bakteriologischen Wasseruntersuchung. [**A Handy Hydro-mechanical Sampling Apparatus for the Bacteriological Examination of Water**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, No. 5/6, 458–62, 3 figs.

A simple apparatus is described which permits precise sampling of water from a deep well for bacteriological analysis. It is both guided and operated by a single cable and can be used with any sample bottle of convenient size provided that this has a stopper that can be gripped by the jaws of the apparatus. The paper is well illustrated by diagram and photographs.

E. Windle Taylor

MCCARTHY, J. A., THOMAS, H. A., Jr. & DELANEY, J. E. **Evaluation of the Reliability of Coliform Density Tests.** *Amer. J. Pub. Health.* 1958, Dec., v. 48, No. 12, 1628–35, 2 figs. [15 refs.]

The 2 general methods of estimating the coliform content of a water sample are the inoculation of multiple tubes of liquid medium to obtain the "most probable number" (MPN) or a direct colony count in a solid medium. There is a considerable error in the MPN estimate, for example, with 5 tubes for each dilution, the figure may be 260% above or 70% below the true count. On the other hand there are serious limitations with the direct colony count method; for example, the amount of sample is very small, other organisms may be erroneously identified as coliform organisms and there is possible inhibition of certain strains when selective media and selective techniques are used.

The precision of plate counts in the range of coliform densities investigated by the authors, however, was found to be at least 3 times as great as the MPN result.

The direct count approach will give even more accurate results with the membrane filter technique.

E. Windle Taylor

LEVIN, G. V., HARRISON, V. R., HESS, W. C., HEIM, A. H. & STAUSS, V. L. **Rapid, Radioactive Test for Coliform Organisms.** *J. Amer. Water Works Ass.* 1959, Jan., v. 51, No. 1, 101–4, 1 fig.

Radio-active sodium formate (0·01%) is incorporated in brilliant-green lactose bile broth.

The medium is shaken for several hours before use in order to reduce non-metabolic $^{14}CO_2$ to a minimum. The shaken medium is introduced into a planchet together with a membrane filter on which the bacteria from the water sample are concentrated. The planchet is placed in ointment jars and incubated at 37°C. for 3 hours. Then a planchet containing several drops of a saturated barium hydroxide solution is added and incubation is continued for another hour. Active carbon dioxide evolved precipitates the barium hydroxide as the carbonate.

At the end of the hour the barium planchet is removed, dried over a heat lamp and counted in an internal-flow Geiger counter.

Investigations are continuing as to the bacteriological efficiency of the formate medium compared with conventional brilliant-green lactose bile broth and as to the possibility of non-coliform organisms producing detectable gas in the radio-activity test.

Initial work on river water and filtered water samples indicates that several non-coliform organisms do interfere. One has been identified as *Pseudomonas pyocyanea.*

A table is given of results with pure cultures of *Escherichia coli* and shows a reasonable degree of correlation between evolved $^{14}CO_2$ and numbers of bacterial cells. *E. Windle Taylor*

FLYNN, J. M., ANDREOLI, A. & GUERRERA, A. A. **Study of Synthetic Detergents in Ground Water.** *J. Amer. Water Works Ass.* 1958, Dec., v. 50, No. 12, 1551–62, 2 figs.

This paper describes an investigation carried out by officials of the Health Department of Suffolk County, New York State, on the occurrence of synthetic detergents in shallow wells. The area of study was in the town of Babylon, Long Island, and covered an area of 72 acres, a mainly residential area built-up to the density of 5–6 houses to the acre. Main services are not available: water comes from shallow wells (14–56 ft. deep) and drainage is apparently to cesspools. The underlying strata are glacial drift, mainly gravel and coarse sand. The general groundwater movement in this area is southwards with a velocity of 1–3 ft. per day.

Attention was first directed to the wells because of complaints of a yellow colour in the well water. This was traced to contamination by hexavalent chromium from a plating factory. This factory is now closed, but the chromium-contaminated water "has continued as a ribbon-like slug in a southerly direction and is now 1,200 ft south of the discharge point and has contaminated six wells in its southward path". [Once again it is astonishing to find in a Long-Island community that contamination of groundwater used for shallow-well supplies by so toxic a material as hexavalent chromium can occur.]

In addition to the wells sampled for chromium 186 wells were sampled for anionic synthetic detergent. 20 well waters were also fully analysed chemically. About one-third of the wells sampled showed the presence of synthetic detergent.

The authors' conclusions may be summarized:

i. Where individual shallow wells and cesspools are placed on relatively small plots it is to be expected that synthetic detergents will be found in the wells.

ii. Increased depth of well or distance between well and cesspool may delay, but is unlikely to prevent, access of these agents to the well water.

iii. The presence of these agents in well water can cause frothing and unpleasant taste (detected by "most persons" at 1·5 p.p.m.).

iv. The householders in the area of study appeared to use about 100 lb. per year of marketed product.

v. The presence of synthetic detergent in well water in such circumstances is a clear indication of sewage contamination.

It may also be wondered what effect these agents have as vehicles for viruses, bacteria etc., and whether the large proportion of phosphates in the marketed products will increase bacterial population and survival time in the shallow aquifer. And, at present, we know little of their long-term toxicity.

[This paper is interesting as a report of an *ad-hoc* study and it serves to stimulate a number of questions. For example, nothing is said about the type of construction of the 186 wells examined. This might well be far more significant than the depth relationship which the authors seek to demonstrate. It would have been valuable, too, to have made a "tracer" study of the groundwater flow to assess the actual dilution so that a calculation could have been made of the "half-life" of these synthetic detergents in groundwater.]

Peter C. G. Isaac

Infestation and Disinfestation

WATSON, W. N. B. **Scabies.** *Med. Officer.* 1958, Nov. 7, v. 100, No. 19, 293–5.

Statistical evidence is given of the decline in scabies in Edinburgh from 1941–2 to 1953–4 and of a comparable decline elsewhere. The evidence also indicates an increase of scabies in Edinburgh and Glasgow in recent years and it is suggested that this will reach its peak in Edinburgh in or soon after 1959–60.

Scabies should be suspected as the cause of any skin complaint and in cases of doubt a therapeutic test should be made with benzyl benzoate.

Investigation and treatment of the family group are the most important measures in combating scabies. When scabies is diagnosed in a child, all child siblings and class-mates should be examined. Even more important is the visitation of the home, which must in every case be made by the health visitor. The contagious nature of the disease must be explained and all inmates with suspicious lesions must be encouraged to seek help either from the local scabies clinic or the family doctor. If the sufferer shares a bed, the other occupant should always be treated at the same time. The value of disinfestation of bedding has been exaggerated. but bedding can transmit scabies, and disinfestation should be done for this reason, and also to reinforce the health education given by the health visitor.

H. T. H. Wilson

SYKES, G. [M.Sc., F.R.I.C.] **Disinfection and Sterilization.**

This book was reviewed on p. 512.

Food and Nutrition

FOODSTUFFS

Composition and Bacteriological Control

PUBLIC HEALTH LAB. SERVICE. **A Search for Organisms of the *Salmonella* Group in Wheat and Flour. A Report.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1958, June, v. 17, 133–5.

Since October 1940 practically every outbreak of paratyphoid fever due to *Salmonella paratyphi B* has been associated with the consumption of synthetic cream, particularly in cream buns. Investigations to demonstrate faecal contamination of the cream were consistently unsuccessful and the suggestion was made by SCOTT THOMPSON [this *Bulletin*, 1954, v. 29, 23] that contaminated flour might be the source of infection.

The widespread enquiry into the contamination of flour which is here reported was undertaken by 18 laboratories of the Public Health Laboratory Service and they examined 2,086 samples of wheat, flour, scourings, offal, dust and other products from 31 mills. No organisms of the *Salmonella* group were found in any of the specimens. *J. Nagington*

PUBLIC HEALTH LAB. SERVICE. **Some Observations on the Bacteriology of Flour. The possible Rôle of Flour in spreading Enteric Disease. A Report.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1958, June, v. 17, 135–46.

During the investigation reported above the opportunity was taken to obtain a general picture of the amount of bacterial contamination of wheat in the milling process.

It was found that 78% of 372 samples of unwashed wheat contained up to over 1,000 coliform organisms per gm. Faecal *coli* (*Escherichia coli* type I) were present in about one-half of one series of 89 samples. These coliform organisms were probably derived partly from the natural flora of the wheat and partly from contamination during and after harvesting. The main source of the faecal *coli* was probably from manured soil and rodent excreta, the latter especially when the wheat was stacked and when the grain was stored.

Over half of the mills examined were found to be using excretally contaminated water to wash the grain. These were mainly the smaller mills—about 80% of the wheat milled in England and Wales is milled by a few large firms who use clean water.

The third and least likely source of contamination was during its handling by human beings. Each of these 3 possible avenues of faecal contamination could lead to the introduction of salmonellae into flour.

Although no salmonellae were grown from the wheat products from the mills *Salmonella paratyphi B* was grown from a rat and an unidentified salmonella was grown from a stoat caught at one mill and *Salm. typhi-murium* was grown from flour at a bakery.

It is concluded that flour is probably seldom responsible for salmonella infections but it should be handled in such a way as to minimize contamination. It is recommended that wheat should be threshed as cut and it should be stored in rat-proof premises. Wheat should be washed with pure water and flour should be kept dry as salmonellae can multiply in it when it is damp. *J. Nagington*

DENNY, C. B.; BOHRER, C. W.; PERKINS, W. E.; TOWNSEND, C. T.; PRATT, G. B.; WHEATON, E. **Destruction of *Clostridium botulinum* by Ionizing Radiation. I. In Neutral Phosphate at Room and Freezing Temperatures** [DENNY, BOHRER, PERKINS & TOWNSEND]. *Food Research.* Champaign, Ill. 1959, Jan.–Feb., v. 24, No. 1, 44–50, 2 figs. [16 refs.] **Part II. Peas, Chicken Soup, and Pork in the Frozen State** [PRATT, WHEATON, BOHRER & DENNY]. *Ibid.*, 51–6, 2 figs.

"Neutral phosphate buffer was used as a standard reference medium for cultures subjected to irradiation. The relationship between irradiation in the reference medium at freezing and room temperatures was discussed. *Cl. botulinum* was shown to be more resistant to radiation in foods than in neutral phosphate when irradiated at freezing temperatures. The use of data obtained from radiation survivor curves was discussed.

"Toxic swells developed in peas inoculated with 10,000 spores per gram of *Cl. botulinum* which had received 2.5 Mrep, but no swell spoilage developed after 3.0 Mrep. Toxic swells developed in similarly inoculated chicken soup which had received 3.5 Mrep, and a non-toxic, putrid swell developed even at 3.6 Mrep, but no swell spoilage developed after 3.8 Mrep. Toxic swells developed in inoculated pork after 3.5 Mrep, and non-toxic swells (one putrid) developed at 3.7 Mrep; no swell spoilage developed after 4.0 Mrep.

"Viable spores were isolated from occasional flat cans of peas and chicken soup incubated one year at 86°C., but in no case was toxin encountered in any flat cans.

"It seems likely that no single dose will be best for all products since resistance of spores is different in different media."

FOOD POISONING

BALICE, A. Salmonellosi "Osimo" 1958. [**An Outbreak of Salmonella Food Poisoning in Osimo, Italy**] *Igiene e San. Pubblica.* Rome. 1958, Nov.–Dec., v. 14, Nos. 11/12, 612–27, 4 figs. [21 refs.] English summary.

Osimo is a commune near Ancona close to the Adriatic coast of Italy and the author describes an outbreak of food-poisoning in which 83 persons living in a farm colony were affected, 12 were children

between 6 and 12 years of age; at least 47 had to be admitted to hospital and 5 died.

Investigations proved that the infecting vehicle was poultry meat eaten at a pre-matrimonial feast (at which the bride's dowry is demonstrated to those interested). The meal was eaten at 1 p.m. and the usual symptoms of vomiting, diarrhoea and fever started 9–30 hours later. Circulatory collapse was a prominent symptom in several patients. 2 children who did not eat the meat but ate other portions of the feast were unaffected, and one person who was not at the meal but who drank out of the same glass as one of the patients also became ill. Necropsy of the 5 fatal cases showed gastro-enteritis with haemorrhagic glomerulonephritis in 2. For the remainder the illness lasted from 1–12 days and the presumed causal organism was isolated from the faeces for at least 30 days after.

After plucking, drawing and cleaning, the poultry were washed in water from an old well not used for drinking, and then were put aside for more than 12 hours in a fairly high ambient temperature before being roasted or boiled. An organism belonging to the *Salmonella* group with B somatic, and e,n,x, flagellar antigens was isolated from the well water, and from the faeces, intestine, spleen and peritoneal fluid of the fatal cases. Blood culture from some of the other patients was negative. Ducks and geese from the farm-yard killed subsequently proved to be healthy carriers of the same organism.

The author considers that these birds infected the well which structurally was in a very poor state, and that the subsequent infection of the cleaned carcasses was favoured by the long time they were kept before cooking. *W. K. Dunscombe*

GREENBERG, R. A., SILLIKER, J. H., NANK, W. K. & SCHMIDT, C. F. **Toxin Production and Organoleptic Breakdown in Vacuum Packaged Fresh Meats inoculated with** *Clostridium botulinum*. *Food Research*. Champaign, Ill. 1958, Nov.–Dec., v. 23, No. 6, 656–61.

In view of the widespread practice of vacuum packaging non-processed perishable foods it was desirable to ascertain whether organoleptically acceptable products could be accepted as free from toxicity. Fresh beef and pork were the meats used, inoculated with definite doses of *Cl. botulinum* spores and the cans were stored at 4 temperatures, 38°, 70°, 85° and 99°F. The tests were the examination of watery emulsions for off-odour and appearance. The cans were packed under anaerobic conditions. The results of incubation at these temperatures are set out in a table.

In no case did detectable toxicity develop before obvious putrefactive breakdown. In some instances putrefaction occurred without the development of toxicity. In other instances an "off" or "sour" type of breakdown resulted but in none of these was toxicity detected. The authors conclude "that the nature of these products combined with the characteristics of *Cl. botulinum* form a system which can be remarkably efficient in warning the consumer of possible hazard in the event of gross mishandling.

W. G. Savage

Bacteriology and Immunity

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-division of this section*

GENERAL

BENEDICT, R. G., CORMAN, J., SHARPE, E. S., KEMP, C. E., HALL, H. H. & JACKSON, R. W. **Preservation of Microorganisms by Freeze-Drying. I. Cell Supernatant, Naylor-Smith Solution, and Salts of Various Acids as Stabilizers for** *Serratia marcescens*. *Applied Microbiol.* Baltimore. 1958, Nov., v. 6, No. 6, 401–7, 4 figs. [14 refs.]

Cultures were grown in a medium containing the solids from skimmed milk, 5%; Protopeptone, 3%; and glucose, 2%. Bacterial cells were washed and resuspended in various solutions ("stabilizer solutions") in which they were freeze-dried. Good survival was obtained when the cells were resuspended in the supernatant fluid in which they had been grown. The paper is devoted to a study of the constituents responsible for this "protective effect" (*i.e.* for the high survival rate), and it was found to reside in a low molecular weight fraction.

Ascorbic acid plus thiourea and ascorbic acid plus ammonium chloride were successful as "stabilizers" in combination, but thiourea alone was almost as efficient. Sodium lactate and sodium acetate at 0·1 M concentrations were also effective. [It should be noted that the results in this paper refer only to survival of the drying process and do not necessarily indicate that the dried products would have high survival rates after storage.] *S. T. Cowan*

MAISTER, H. G., PFEIFER, V. F., BOGART, W. M. & HEGER, E. N. **Survival during Storage of *Serratia marcescens* dried by Continuous Vacuum Sublimation.** *Applied Microbiol.* Baltimore. 1958, Nov., v. 6, No. 6, 413–19, 3 figs. [12 refs.]

This paper reports experiments to determine factors affecting the storage life of freeze-dried cultures of a bacterium. The results confirm facts already well known. (1) Few cells survived when the residual moisture was 2% or more; the optimal concentration is about 0·5–0·6%. (2) Cultures grown for 24–28 hours survived better than those grown for only 16–20 hours. (3) Survival was better at 35°C. than at 80°C.; in fact over 70°C. survival was measured in hours rather than weeks. (4) Survival time at high temperatures could not be correlated with survival time at normal storage temperature. An unexpected finding was that survival was as good in nitrogen as in a vacuum; this was explained by difficulty in sealing tubes. [The storage life investigated here was limited to 6 months at 20°C., or 12 months at −18°C.] *S. T. Cowan*

HABEEB, A. F. S. A. **A Study of Bacteriological Media; the Examination of Bacto-Casitone.** *J. Pharmacy & Pharmacol.* London. 1959, Mar., v. 11, No. 3, 157–62, 1 fig. [18 refs.]

"Three batches of Bacto-Casitone have been examined quantitatively for their free and total amino acids using paper chromatography. Variation occurs in the free amino acids in the three batches. The spots due to the peptides have been found to be a mixture of peptides. When casitone was examined for its streptogenin activity using the medium of Steele, Sauberlich, Reynolds and Baumann, and Kodicek and Mistry the stimulatory pattern in the two media appeared to be different. The three batches showed similar streptogenin activity."

MEYNELL, G. G. & MEYNELL, Elinor W. **The Growth of Micro-Organisms *in vivo* with particular Reference to the Relation between Dose and Latent Period.** *J. Hygiene.* 1958, Sept., v. 56, No. 3, 323–46, 12 figs. [Numerous refs.]

The hypothesis of independent action suggests that the characteristic dose/mortality curve when an animal is inoculated with a progressively increasing number of pathogenic organisms can best be explained by the assumption that the increasing size of inoculum enhances the probability of a single, effective organism multiplying to the stage at which death of the animal occurs. An alternative explanation is that all the cells in the inoculum act synergically. In an earlier paper [this *Bulletin*, 1957, v. 32, 599] partial agreement was found between experimental results and those postulated by the "independent hypothesis".

In the work reported here further tests of the hypothesis are undertaken. The relation between size of inoculum and latent period, and the growth of organisms *in vivo*, are investigated by inoculating mice with several strains of *Salmonella typhi-murium*. A mathematical model is used; this postulates that the organisms causing a response (death in this case) increase *in vivo* at a rate which is constant for all doses and that the response is certain to occur when their number reaches a critical value. Viable counts on pooled viscera suggest that the model is valid. This being so, the hypothesis of independent action could be tested by determining the relationship between dose and latent period for doses of less than 1 ED50. According to the hypothesis, the latent periods for different doses smaller than 1 ED50 should be the same since the critical number of organisms would be achieved by the multiplication of a single cell. In the few instances reported here in which a series of doses lower than 1 LD50 are administered the latent periods are, in fact, roughly similar.

The findings in experiments in which partially resistant mice are used (LD50 = $10^{2\cdot5}$–10^{6} organisms) do not fit the hypothesis which states that only a fraction of the inoculum usually initiates the response. Viable counts indicate that the number of organisms present at death corresponds to the growth of all the organisms inoculated and not to that of a postulated effective fraction. [It seems from the results of growth experiments *in vivo* that the hypothesis of independent action can only be made to fit the observations by modifications which make it indistinguishable from its alternative—the hypothesis of synergic action.] *R. B. Morrison*

KRAFT, Lisbeth M. **Observations on the Control and Natural History of Epidemic Diarrhea of Infant Mice (EDIM).** *Yale J. Biol. & Med.* 1958, Dec., v. 31, No. 3, 121–37, 4 figs. on 2 pls. [10 refs.]

This paper describes the method adopted to control an air-borne virus infection which causes epidemic diarrhoeal disease in infant mice. The principle of the method consisted of transferring females, as soon as they were observed to be pregnant, to specially devised "filter cages" where the litters were born and cared for under the strictest precautions until the litter in each filter cage was 12 days old—past the danger period. By this means the author was successful in breeding a colony free from epidemic diarrhoea. It is a difficult paper to abstract and the reader is referred to the original for details. *H. J. Bensted*

MURRAY, E. G. D., DENTON, G. D., STEVENSON, J. W. & DIENA, B. B. **A Toxin-Inactivating Substance (Noxiversin) from *Penicillium cyaneo-fulvum* (Biourge).** *Canadian J. Microbiol.* Ottawa. 1958, Dec., v. 4, No. 6, 593–609. [25 refs.]

The mould producing this substance was a contaminant in a culture of sputum made for the isolation of tubercle bacilli, and attention was directed to its toxin-inactivating properties by the observation that the growth of a penicillin-resistant staphylococcus, although unimpeded by the presence of the mould, produced no haemolysis on blood agar. It also produces an antibiotic with a similar spectrum to that of penicillin, but this and the toxin-inactivating substance are distinct. The latter substance was concentrated from cultures in glucose-beef-infusion broth: the product obtained consisted of carbohydrate and protein, the second being

the active principle. This was found to be thermolabile, to be removed by Seitz filtration (apparently owing to adsorption) and to be completely inactivated by serum albumin.

Noxiversin was shown by *in vitro* tests to neutralize the haemolysins of *Staphylococcus aureus* (α and β) *Streptococcus pyogenes* (S and O), *Clostridium welchii*, *Cl. septicum*, *Cl. histolyticum* and *Cl. tetani*. It was also shown by tests in mice to be capable of neutralizing the neurotoxin of *Cl. tetani*, and some experiments of which no details are given suggest an action on the toxin of *Corynebacterium diphtheriae*. [Remarkably large amounts of the substance apparently had to be used in the *in vitro* tests: the standard addition of noxiversin was 150 mgm., and although this neutralized 3,520 units of staphylococcus α lysin, the number of units of other toxins neutralized by it varied from 512 to only 8.] Toxin neutralized with noxiversin retained its antigenicity: *i.e.* noxiversin is a "toxoiding" agent, and clearly acts directly on toxin, and not in any intermediate way. *L. P. Garrod*

FANINGER, A. & MISKOV, D. Ispitivanje bakteriske flore kod osoblja bolnice u Zrenjaninu. I. Saopštenje. [**Examination of the Bacterial Flora of the Staff in the Hospital at Zrenjanin. I. Communication**] *Higijena.* Belgrade. 1958, v. 10, No. 2, 137–44. [11 refs.] English summary. II. Saopštenje. [**II. Communication**] *Ibid.*, 145–50. English summary (9 lines).

Between March and June 1957 an examination was made of the bacterial flora of the nasopharynx in 269 members of the staff of the hospital at Zrenjanin, Yugoslavia. Haemolytic *Staphylococcus albus* was found in 41 (15·2%) haemolytic *Staph. aureus* in 23 (8·5%) and β-haemolytic streptococci in 23 (8·5%) and *Klebsiella pneumoniae* in 10 (3·7%) persons. At an examination carried out subsequently on the same 83 persons from whom the pathogenic organisms were isolated only 24 were found to be still infected. In examinations of the samples taken at various points throughout the hospital haemolytic *Staph. albus* was isolated on 27 and haemolytic *Staph. aureus* on 12 occasions. In June and July 1957 pathogenic staphylococci were also isolated in a similar examination carried out in the dermatological and venereal diseases department and children's department of the same hospital. *D. J. Bauer*

RIDLEY, M. **Perineal Carriage of** *Staph. aureus.* *Brit. Med. J.* 1959, Jan. 31, 270–73.

52% of 50 male medical students had no coagulase positive staphylococci in their noses and on the skin. 26% had many organisms in the nose and a few on the perineal skin. 12% were heavy nasal and perineal carriers and 10% were heavy perineal carriers only. 5 of 12 perineal carriers remained heavy carriers over 6 weeks to 6 months, 5 became non-carriers and one non-carrier subsequently became a heavy perineal carrier. Double nasal and perineal carriers had strains of the same phage type in both sites and these types persisted. Perineal carriers continued to carry strains of the same type. The distribution of phage types from the perineum was similar to the distribution in nasal carriers.

Experiments showed that dispersal of organisms into the air by perineal carriers was variable as is dispersal by nasal carriers. There was good correlation between degree of dispersal and the number of staphylococci isolated from the carriers' clothing and fingers.

Faecal staphylococci, when present, were of the same phage type as those on the perineal skin but faecal contamination alone was not responsible for the perineal staphylococci since 5 of 9 heavy carriers were not faecal carriers. Multiplication of the organism on the perineum is suggested to account for its persistence over a long period of time. *M. Patricia Jevons*

KNIGHTS, H. T. **The Air Hygiene of Obstetrical Unit Nurseries. A Preliminary Study.** *New. Zealand Med. J.* 1958, Oct., v. 57, No. 321, 487–95, 2 figs. on pl. & 1 graph. [33 refs.]

Air samples were taken for bacteriological examination in 18 maternity unit nurseries in 15 New Zealand hospitals. The slit sampler was employed to collect air bacteria on agar containing phenolphthalein phosphate. The count varied greatly with the activity in the nursery and "total bacteria" averaged 203 colonies per cu.ft. during bathing; during quiet periods the count was about 24. Numerous staphylococci of phage type 80/81 were found in the samples. When cot bathing was substituted for bathing in a communal sink the count was much lower. Staphylococci of the epidemic type could be demonstrated at least 12 feet from the source of dispersal.

The importance of the umbilicus as a site of silent staphylococcal infection, and as a source for dispersal into the environment, was confirmed.

On several occasions the air samples were found to contain staphylococci of a type carried by the operator of the sampler; the importance of typing the staphylococci before interpreting the results is therefore clear. *R. E. O. Williams*

WALTER, C. W., RUBENSTEIN, A. D., KUNDSIN, Ruth B. & SHILKRET, Mary A. **Bacteriology of the Bedside Carafe.** *New England J. of Med.* 1958, Dec. 18, v. 259, No. 25, 1198–202.

The water in bedside carafes in 24 Boston hospitals was examined bacteriologically, and a questionary form involving 47 observations was compiled. 22% of the samples yielded coliform organisms, in most cases less than 50 per ml. and 70% yielded "staphylococci". At least one strain of *Staphylococcus aureus* phage type 80/81 was isolated.

Opportunities for contamination of the carafes were numerous, and included: the habit of replenishing, rather than emptying and refilling; difficulty of cleaning carafes of the usual shape; repeated contamination during drinking; frequent absence of any disinfection routine; the use of contaminated ice, or its contamination during transfer to the carafe. It is recommended

that steps be taken to mitigate these hazards, to institute regular bacteriological testing of the carafe water, and to restrict the supply of bedside carafes to bedridden patients. *R. E. O. Williams*

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

In this section the abstracts are arranged as far as possible in the following order:—General; Antibiotics; Other Therapeutic substances; Disinfection.

WALTER, Anneliese & MARGET, W. Eine Mikromethode, geeignet zur Bestimmung von Blut-Konzentrationen der meisten gebräuchlichen Antibiotica. Unter Ausnutzung des beobachteten Hemmeffektes von Hämoglobin gegenüber Bakterien. [**A Micro-Method suitable for estimating the Blood Concentration of Antibiotics in Common Use. Utilization of the Observed Inhibitory Effect of Haemoglobin on Bacteria**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 4, 320–30, 2 figs.

This paper is from the University Children's Clinic in Freiburg, and the method described obviates the necessity for venepuncture. 2 0·03 ml. samples of blood are transferred by pipette to filter paper disks containing liquoid to prevent clotting, and these are dried. They are then placed on the surface of agar pre-seeded with *Bacillus subtilis* for assays of penicillin or chloramphenicol, or *B. cereus* for tetracycline. Other disks contain known amounts of the antibiotic together with the same quantity of normal blood: a standard curve is plotted from the inhibition zone diameters produced by these and the unknown is read from this in the usual way. The control disks must also contain blood because its presence increases the diameter of the inhibition zone produce, and may make a difference between having a measurable zone and none at all (such differences are illustrated). Some tests are described which show that this effect, which increases the sensitivity of the assay method, is due to haemoglobin. A modification enabling lower concentrations to be detected is to add a known amount of antibiotic to the test disks (*e.g.*, 25 μgm. chloramphenicol) and to deduce the amount also present in the contained blood from the difference between the zone diameter and that given by the 25 μgm. control [might not the use of a more sensitive organism for this assay be preferable?]. Only the 3 antibiotics already mentioned are referred to and no actual results are given.

L. P. Garrod

OLBERG, H. Über den Einfluss eines nichtionogenen Netzmittels auf einige gebräuchliche Antibiotika (In-vitro Teste). [**On the Influence of a Non-ionic Wetting-Agent on some Commonly Used Antibiotics (*In vitro* Tests)**]. *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 1/2, 141–50, 10 figs. [17 refs.]

The author is Scientific Director of the Lyssia-Werke, Wiesbaden, manufacturers of a preparation (Fugin) used in these experiments. Surface-active substances are sometimes added to solutions of antibiotics to be administered by inhalation, and the purpose of these experiments was to determine what effect they may have on the activity of the antibiotics. Two such substances were tested, polyoxyethylated castor oil (PR), and Fugin, which contains polyoxyethylated castor oil and unstated quantities of 2-ethoxy-6,9-diamino acridine lactate and of emulsified essential oils. The method of test was to determine the minimum inhibitory concentration of the antibiotics in broth for each of 3 organisms, *Staphylococcus aureus, Streptococcus pyogenes* and *Escherichia coli* in the absence of and in the presence of different amounts of PR and Fugin diluted in both distilled water and saline: the tubes were also subcultivated to determine what concentrations were bactericidal. PR reduced the activity of tyrothricin, enhanced that of penicillin and tetracycline, and did not affect that of bacitracin, neomycin, oleandomycin or dihydrostreptomycin. Some results are also given for a proprietary mixture of several antibiotics and of an antibiotic with other substances. Fugin enhanced the activity of every antibiotic tested, sometimes to a considerable degree. [The author offers no specific explanation for this. The most probable one appears to be the added effect from the acridine compound contained in it. These compounds are powerful bacteriostatic agents, and a test with Fugin alone was not included in the experiments: apparently contradictory statements about its action are made in the introduction, namely, that 1, 2 and 4% solutions had no inhibitory action on any of the 3 organisms, and that its minimum inhibitory dilution for the streptococcus ("subculture"—? meaning bactericidal dilution) was 1 in 1024.] *L. P. Garrod*

BECHTLE, R. M. & SCHERR, G. H. **A New Agar for *in Vitro* Antimicrobial Sensitivity Testing.** *Antibiotics & Chemotherapy.* New York. 1958, Dec., v. 8, No. 12, 599–606, 4 figs. [42 refs.]

This paper from the Department of Microbiology in the University of Illinois commends an agar of British manufacture for preparing media for certain antibiotic sensitivity tests. Polypeptide antibiotics and others having large molecules diffuse poorly in ordinary media, and disks containing reasonable amounts may produce an unduly narrow zone of inhibition or none at all. In medium solidified with 0·75% of Ionagar 2 (Oxo Ltd., London), which has the same consistency as that given by 1·5% of conventional agar, this difficulty is overcome: a zone of inhibition was obtained from a disk containing only 10 μgm. of polymyxin, whereas one containing 50 μgm. did not produce one on ordinary medium. Results with bacitracin were similar, and a smaller difference of the same kind was observed with ristocetin. The new agar makes little difference to the results with more readily diffusible antibiotics and with sulphonamides: it is suggested that penicillin zones may even be slightly smaller because more rapid diffusion dilutes it to the point of inactivity, but the actual differences observed with penicillin, erythromycin, chloramphenicol and sodium sulphadiazine are so small as

to seem of doubtful significance. There are good photographs of plates illustrating these findings.

L. P. Garrod

STAPLEY, E. O. **Cross-Resistance Studies and Antibiotic Identification.** *Applied Microbiol.* Baltimore. 1958, Nov., v. 6, No. 6, 392–8, 4 figs.

This paper from the Research Laboratories of Merck, Sharp and Dohme, Rahway, N.J., is concerned with a well known method of provisionally identifying an unknown antibiotic as one already known, namely by testing its action on strains of organisms both sensitive and resistant to known antibiotics. In these experiments a single strain of *Escherichia coli* was rendered resistant to 12 antibiotics, and the most original feature of the work was the method used for this: it consisted of continuous culture in an apparatus (illustrated) permitting the periodical addition of antibiotic followed by successive additions of fresh medium until the most resistant cells were able to resume growth. In this way increases in resistance varying from 125- to 2,500-fold were obtained for 11 antibiotics: the increase for grisein is not stated. Cross-resistance studies then gave some peculiar results, which seem to suggest that this method has very limited value. The only antibiotic unrelated to any other was grisein. Organisms rendered resistant to pleocidin, neomycin and viomycin were resistant to all 3 of these and to streptomycin, streptothricin and cycloserine. There was complete cross-resistance between chloramphenicol and the 3 tetracyclines. Resistance to polymyxin was accompanied by resistance to streptomycin and streptothricin. Some of these relations are "one-way". The results of testing 8 other antibiotics with these 12 resistant strains are also given: thioaurin showed no definite relationship with any of them, but cross-resistance with one or more of the others was found for streptolin A and B, streptin, soframycin, netropsin, xanthomycin, hygromycin and albomycin. The use of paper strip chromatography for identifying antibiotics, and particularly mixtures of antibiotics, is also described. *L. P. Garrod*

ROCHA, H. & GUZE, L. B. *In vitro* **Sensitivities of Gram-Negative Bacteria to Combinations of Antibiotics. Observations on the Use of the Antibiotic-Strip Replica-Plating Technic.** *Amer. J. Clin. Path.* 1958, Nov., v. 30, No. 5, 463–9, 3 figs. [24 refs.]

These authors have tried to determine the nature of combined antibiotic action by the right angle paper strip method, in which such action is judged by the contour of the inhibition zone in the angle between the 2 strips, where the antibiotics are diffusing together. They also made replica plates from such cultures, but although they include this process in the title of their method, it seems only to have shown that bactericidal antibiotics are bactericidal and others are not: such results are referred to in only 5 lines of text, and it seems that conclusions about the effect of different combinations are based on appearances in the primary culture.

The organisms studied were 149 strains of coliform bacilli (*Escherichia coli, Proteus, Pseudomonas,* etc.), and the antibiotics were streptomycin, neomycin, chloramphenicol and the 3 tetracyclines: Furadantin was also included. Of the 10 combinations of these studied, none gave consistent results against all species, and the only type of effect ever consistently found against any single organism was "no interaction". Some results were very varied: neomycin + oxytetracycline showed no interaction in 71 instances, synergy in 22 of which 13 were *E. coli,* and antagonism in 26 of which 16 were *Proteus.* Quite inexplicably, in view of the latter result, the very closely related combination neomycin + chlortetracycline showed synergy against 16 strains of *Proteus* and antagonism with none. No interaction was much the commonest finding. Other combinations for which antagonism was a commoner finding than synergy were streptomycin + oxytetracycline and Furadantin + oxy- or chlortetracycline. [It seems impossible to draw any general conclusions from such findings, and the validity of the method as a clinical guide remains unproven.] *L. P. Garrod*

FEHR, A. M. Das Problem der therapieresistenten Kokkenstämme in der Chirurgie. [**The Problem of Drug Resistant Cocci in Surgery**] *Schweiz. med. Woch.* 1959, Jan. 17, v. 89, No. 3, 89–91. [16 refs.]

This paper by the Director of the Surgery Clinic of the Canton Hospital at Winterthur is a general discussion on the problem of cross-infection, particularly by staphylococci, in surgical wards at the present day, with few facts from his personal experience except some information about the frequency of antibiotic resistance in strains of staphylococci from lesions and carriers [lower than has been reported from elsewhere] and the mention of 6 fatal cases of acute enterocolitis since 1955. The remedies suggested are more stringent aseptic precautions, some common lapses in connexion with which are cited, and the more restricted use of antibiotics, particularly in prophylaxis. Rapidly extending carbuncle of the face and acute haematogenous osteomyelitis in children are among the few conditions demanding immediate antibiotic treatment: in most others treatment should be based on the results of cultivation and sensitivity studies. Dosage must be adequate, and penicillin, when at all applicable, is to be preferred to the broad spectrum antibiotics, which are "held in reserve". *L. P. Garrod*

BARBER, Mary, CSILLAG, Anna & MEDWAY, A. J. **Staphylococcal Infection resistant to Chloramphenicol, Erythromycin, and Novobiocin. Effect of Antibiotic Combinations on the Emergence of Resistant Strains.** *Brit. Med. J.* 1958, Dec. 6, 1377–80, 1 chart. [21 refs.]

This paper reports some early results of a clinical experiment at the Hammersmith Hospital (British Postgraduate Medical School). It was decided to observe the effect on antibiotic resistance in staphylococci of (1) abandoning the use of penicillin except in certain specified wards and (2) prescribing antibiotics only in combination with another antibiotic or a sulphonamide.

The findings are given for 1 year, the first 6 months of which were before this policy was introduced: during the whole period 982 staphylococcal infections occurred. The frequency of resistance to both penicillin and tetracycline diminished substantially throughout the year [but since the fall seems to have been at a similar rate in both halves of the year it presumably cannot be credited to the new policy]. The frequency of resistance to other antibiotics remained comparatively low, only that to erythromycin showing a slight increase.

The features in their results on which the authors lay most emphasis appear to afford evidence of cross-resistance between erythromycin and chloramphenicol. 44 infections, shown by phage typing to be due to 23 different strains, were erythromycin-resistant and 8 of these organisms were also chloramphenicol-resistant. From 30 infections, again due to 23 different types, the organism was chloramphenicol-resistant, and again 8 of these were erythromycin-resistant. Some of these patients had received both antibiotics, but 1 with chloramphenicol-resistant organisms had been given only erythromycin, and 3 with erythromycin-resistant organisms had received only chloramphenicol. This combination is therefore condemned as unsatisfactory. Although many more patients (108 in contrast to 69) were given erythromycin + novobiocin, none of their staphylococci became resistant to erythromycin and only 2 to novobiocin. [Nothing is said about dosage. According to some authorities (*e.g., New England J. of Med.*, 1956, v. 255, 1057) when 2 antibiotics are used together, each should be given in the same dose as that indicated were it prescribed alone. In interpreting the results of such clinical trials it is necessary to know whether this principle has been observed.]

L. P. Garrod

Hsie, Jen-Yah, Nusser, W., Epstein, S., Van Maren, H. & Ozog, S. **Staphylococcal Resistance to Ristocetin, Oleandomycin, and Novobiocin.** *Antibiotics & Chemotherapy.* New York. 1958, Dec., v. 8, No. 12, 607–14, 6 figs. [10 refs.]

Resistant variants of strains of *Staphylococcus aureus* originally sensitive to the 3 antibiotics studied were obtained by plating a heavy inoculum on agar containing different concentrations and subcultivating colonies from the plate containing the highest concentration yielding growth. (The authors commend this in preference to the "serial transfer" method, presumably in broth.) At each stage the distribution of resistance was studied on gradient plates. [In studying the graphic illustrations of this the reader interested in the numerals on the abscissa of Fig. 2 or in the symbols used in Fig. 6 should provide himself with a powerful magnifying glass.] Whereas a 1,000-fold increase of resistance to novobiocin was obtained in 5 steps and to oleandomycin in 3, 10 steps produced only a 5-fold increase of resistance to ristocetin. Some information is also given about cross-resistance to erythromycin and carbomycin in strains with induced resistance to oleandomycin [why strains Y and S are stated in Table III to have increased only 5–20-fold in resistance to oleandomycin, whereas the increase is said earlier to have been 1,000-fold, is not explained], and about cross-resistance between novobiocin and oleandomycin and 8 other antibiotics in 98 recently isolated strains not artificially habituated to any antibiotic.

L. P. Garrod

Davis, A., Ramsay, A. M. & Mann, A. J. **Resistant Staphylococcal Puerperal Septicaemia susceptible to Vancomycin.** [Memoranda.] *Brit. Med. J.* 1958, Dec. 6, 1394, 1 chart.

A woman aged 40 pregnant for the 10th time had ruptured membranes 11 weeks before her delivery date, and was spontaneously delivered of a macerated foetus 9 days later. There was high fever just before labour which subsided but recurred 2 days later: staphylococci were cultivated from a vaginal swab and from the blood. Treatment with oxytetracycline, penicillin, erythromycin and chloramphenicol had no apparent effect, a high remittent fever with rigors persisting, together with liver enlargement and the development of anaemia and signs suggesting endocarditis. 16 days after delivery treatment was begun with vancomycin 500 mgm. intravenously at 8-hour intervals. Fever abated immediately and uninterrupted and complete recovery followed.

L. P. Garrod

Fürész, S., Zangaglia, O. & Scotti, R. **The Effect of Fixed Combinations of Antibiotics on Staphylococci** *in Vitro. Antibiotics & Chemotherapy. New York.* 1958, Nov., v. 8, No. 11, 571–5, 6 figs. [12 refs.]

The sensitivity of 58 strains of *Staphylococcus aureus* and of strains of *Staph. albus* to 5 antibiotics was tested by the tube dilution method in dextrose broth. The antibiotics were tested individually and in the following fixed combinations: novobiocin and tetracycline (1 : 2) chloramphenicol and tetracycline (1·5 : 1) tetracycline and oleandomycin (2 : 1) novobiocin and penicillin V (1 : 1) and novobiocin and chloramphenicol (1 : 2).

All combinations inhibited more strains than the component members separately. The highest inhibitory power was obtained with the mixture of novobiocin and tetracycline, all strains tested being inhibited by a concentration of 3 μgm./ml.

M. Patricia Jevons

Sleigh, J. D. **Difficulties encountered in reporting the Penicillin Sensitivity of Staphylococci.** *Scottish Med. J.* Glasgow. 1958, Nov., v. 3, No. 11, 454–9, 4 figs.

Irregular results obtained with penicillin sensitivity tests in primary cultures of material containing staphylococci led to an examination of the commercial 0·5 unit tablets used. 5 batches were compared by 3 methods; by placing one of each batch on plates sown with sensitive and resistant strains and by dissolving tablets and assaying their penicillin content by both a tube dilution method and a cup plate diffusion method with *Bacillus subtilis*. The actual content of the "0·5 unit" tablets was found to vary from 0·1 to 4 units: none had reached their expiry date and there was no

apparent relation between age and penicillin content. A tablet containing 4 units can produce a wide inhibition zone in a lightly sown plate of a penicillin-resistant staphylococcus, but a resistant (penicillinase-forming) strain can be distinguished from a sensitive one by the size of the colonies bordering the inhibition zone. [This method of distinction was first described, and illustrated as in this paper, by WATERWORTH (*Ann. Inst. Pasteur*, 1948, v. 75, 94).] *L. P. Garrod*

WATSON, K. C., JOUBERT, S. M. & BENNETT, M. A. E. **Penicillin as an Antigen.** [Correspondence.] *Nature.* 1959, Feb. 14, v. 183, 468–9.

These authors have confirmed some of the observations of LEY *et al.* [this *Bulletin*, 1958, v. 33, 1072] on the occurrence and properties of an antibody to penicillin in some human sera. Of 1,200 specimens, 18 agglutinated group O Rh-negative cells which had been suspended in a solution of penicillin. One serum with particularly high activity, from a patient who had had a long course of penicillin treatment (eventual haemagglutinin titre was 1,000) was studied in detail. It was confirmed that treatment of the serum with penicillin abolishes its haemagglutinating activity, but it was not confirmed that haemagglutination can be obtained with the antiglobulin test. By starch gel electrophoresis the antibody was detected in the 2 pre-albumin zones. The effect of penicillinase on penicillin-sensitized cells was also studied: treatment with this only delayed haemagglutination and did not destroy the penicillin.
L. P. Garrod

OLITZKI, A. L. & OLITZKI, Z. **Quantitative Determination of Streptomycin in Organs after Subcutaneous and Intraperitoneal Injections with the Aid of a Streptomycin-Dependent** *Vibrio comma. Bull. Res. Counc. of Israel.* 1958, Oct., v. 7E, No. 3, 171–4, 1 fig.

This paper describes an ingenious method of assaying streptomycin, but without offering evidence that it is more accurate, sensitive or convenient than conventional procedures. Organs were removed from mice at intervals varying from 15 minutes to 3 days after an injection of streptomycin and ground in saline to produce a measured w/v suspension (in Table 1, column 2, "μg." should be "mg."). Dilutions of this suspension were placed in cups in a plate of a starch-containing medium inoculated with a streptomycin-dependent *Vibrio comma* [*cholerae*]. After incubation the plates were flooded with iodine: a zone surrounding the cup was colourless, diffusion of streptomycin having permitted growth and thus decomposition of the starch, and the width of this zone was an index of the streptomycin content. The amounts found are stated for 11 time intervals after subcutaneous injection and 9 after intraperitoneal. Disappearance was more rapid after injection by the latter route. The authors draw attention to the persistence of the antibiotic in the spleen and lungs after it has disappeared from the blood and kidneys, but some of the figures do not bear this out; much more remarkable are the very small amounts detected in the liver. *L. P. Garrod*

OPARA, Z. **Effect of Chloromycetin on the Transformations of Streptomycin Resistance in Pneumococci.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1958, v. 6, Nos. 11/12, 471–4, 1 fig. [10 refs.]

A transforming agent extracted from a streptomycin-resistant variant of type II pneumococcus when added to a culture of the parent sensitive strain caused a rapidly increasing proportion of the cells in this culture to become resistant to streptomycin. This change could be almost completely prevented by the addition of 10 μgm./ml. of chloramphenicol, a concentration which inhibits growth without killing, but the addition had to be made within 30 minutes after mixing culture and transforming agent. According to the author "this result proves that protein synthesis is essential in this period for producing a new characteristic".
L. P. Garrod

DUB, O., RATHOVÁ, Eva & RATH, R. Zpráva o 800 nemocných léčěných chloramfenikolem bez závažnějších komplikací. [**Report on 800 Patients treated with Chloramphenicol without Serious Complications**] *Časopis Lékařů Českých.* Prague. 1958, Sept. 19, v. 97, No. 38, 1197–1202. [17 refs.] English summary.

Treatment with chloramphenicol was carried out on 256 patients suffering from chronic unspecific respiratory infection; 48% showed a marked improvement, and the condition remained unchanged in only 5%. A further group of 544 patients, including also 75 suffering from urinary infection and 22 with cholecystitis, were also treated with chloramphenicol. Treatment was continued for 13–15 days, and the total dose ranged from 6 to 44 gm. with an average of 14·3 gm. The drug was well tolerated, and side effects were only observed in 18 patients (3.9%), 13 of whom developed a morbilliform exanthem, 2 nausea and 3 diarrhoea. The exanthem appeared on the trunk and arms and spread rapidly; it consisted of itching red macules, and disappeared rapidly when treatment with chloramphenicol was discontinued. The authors conclude that treatment with chloramphenicol is without danger when properly controlled, and that the drug should therefore be used more extensively. *D. J. Bauer*

BLASS, R. Klinische Erfahrungen mit dem Antibioticum Sigmamycin unter besonderer Berücksichtigung seiner Wirkung auf die Darmflora. [**Clinical Experiences with the Antibiotic Sigmamycin with special reference to its Action on the Intestinal Flora**] *Schweiz. med. Woch.* 1959, Feb. 7, v. 89, No. 6, 158–61. [Numerous refs.]

This paper from the University Surgical Clinic at Zürich reports the effect of using Sigmamycin (a mixture of tetracycline and oleandomycin) as a regular antibiotic in surgical cases for both prophylaxis and therapy. The author previously used penicillin + streptomycin (doses not stated) in the same way: there is no mention of varying the treatment according to the

nature of the infection or the results of sensitivity tests. Sigmamycin, usually in doses of 500 mgm. 3 times a day, was given to 93 patients in whom treatment with penicillin and streptomycin had failed, and to 24 previously untreated. A table gives diagnoses, the infecting organisms (most often staphylococci) and the results of treatment. In 15 patients the administration was prophylactic: others had wound infections, urinary tract infections, pneumonia, peritonitis and various other septic conditions. Treatment was successful in 98 patients, failed in 7, with apparently doubtful results in 12. Quantitative cultures were made to determine the effect on the aerobic flora of the faeces: this was sometimes much reduced, but only 3 patients had diarrhoea. No details of these results are given, but there are particulars of the frequency with which staphylococci, *Candida* and *Proteus* were found before, during and after treatment: these organisms most often appeared during treatment and disappeared afterwards.

L. P. Garrod

Koch, R. & Asay, L. D. **Oleandomycin, a Laboratory and Clinical Evaluation.** *J. Pediatrics.* St. Louis. 1958, Dec., v. 53, No. 6, 676–82, 6 figs. [14 refs.]

These studies were carried out at the Los Angeles Children's Hospital. Oleandomycin phosphate was administered by intravenous, intramuscular or slow subcutaneous injection, and triacetyl oleandomycin by the mouth. Serial assays of the antibiotic content of the blood were made after single doses of 25 mgm./kgm. body weight given by each of these 4 routes: high levels (5–40 μgm./ml.) were found in the first 2 hours, falling until the 8th or 9th hour to an extent varying with the route of administration: in 4 subjects cerebrospinal fluid was also examined and found to contain 2·5 or 5 μgm./ml. when the blood content was 20 μgm./ml. [Neither the number of patients used in these tests nor their ages are stated. Each graph giving the results represents 16–20 venepunctures: Californian children are evidently tough.]

The rather large standard dose of 100 mgm./kgm. body weight per day was adopted for all routes for therapeutic purposes: 45 patients received this by continuous intravenous infusion for an average of 6 days, 67 received it by intramuscular injection and 82 by mouth at 6-hour intervals for an average of 5 and 5·8 days respectively and 5 were given it by subcutaneous infusion. The results in 86 of these patients who were given oleandomycin alone, mainly for staphylococcal infections, are stated: 80 were cured. Local reactions were sometimes caused by intramuscular injections, and 3 patients treated for 12, 14 and 35 days developed jaundice. Of 328 strains of staphylococci, 26 were resistant to erythromycin but only 6 to oleandomycin.

L. P. Garrod

Nara, T. & Johnson, M. J. **Production, Purification, and Characterization of Synnematin.** *J. Bacteriology.* 1959, Feb., v. 77, No. 2, 217–26, 4 figs. [25 refs.]

Fairbrother, R. W. & Williams, B. L. ***In-vitro* Activity of Ristocetin and Framycetin. Two New Antibiotics.** *Lancet.* 1958, Dec. 27, 1353–5.

These authors determined the minimum inhibitory concentrations of ristocetin and framycetin for multiple strains of staphylococci, streptococci, pneumococci and several varieties of coliform bacilli, with results generally in accordance with the findings of previous authors. The 2 antibiotics are almost equally active against staphylococci and pneumococci, but ristocetin is much the more active against streptococci (*Str. pyogenes* or *faecalis*), whereas only framycetin had any demonstrated activity against "coliforms", *Proteus* and *Pseudomonas pyocyanea.* They also tried to habituate several strains of *Staphylococcus aureus* and *Ps. pyocyanea* to framycetin, and of *Staph. aureus* and 1 of *Str. faecalis* to ristocetin. Resistance was readily developed to the former but very little to the latter. *L. P. Garrod*

Martin, A. R. **A Technique for Studying the Action of Antiseptics on Bacteria in Subcutaneous Tissues, with special reference to Chlorhexidine.** *J. Clin. Path.* 1959, Jan., v. 12, No. 1, 48–51. [15 refs.]

The technique described is the subcutaneous injection of a fatal inoculum of *Streptococcus pyogenes* in anaesthetized mice, the needle being left *in situ* and antiseptic injected through it 20 minutes later. Variations of it include delaying the antiseptic injection for 1, 2, 4 or 6 hours, preparing both inoculum and antiseptic in blood instead of broth or water, and injecting the "antiseptic" elsewhere, which had no effect unless this was an antibiotic or a sulphonamide. In the doses used, chlorhexidine was the most effective antiseptic tested, sometimes giving nearly 100% survival under the more favourable conditions. Several quaternary ammonium compounds, and a solution of *m*-chloroxylenol, had little or no effect: 3 antibiotics, sulphadimidine, proflavine hemisulphate and iodine (in water; there was almost no effect in blood) were intermediate in protecting power. *L. P. Garrod*

Sprössig, M. Austestung virusinaktivierender Eigenschaften von Desinfektionsmitteln im exembryonierten Brutei. [**The Testing of Virus-Inactivating Properties of Disinfectants in Embryonated Eggs**] *Arch. f. Hyg. u. Bakt.* 1958, Sept., v. 142, No. 6, 425–40, 2 figs. [98 refs.]

Virus suspensions were mixed with solutions of 9 disinfectants, and after 2 minutes greatly diluted and introduced into eggs from which the embryo had been removed. Samples were then removed at intervals for titration of haemagglutinin, indicating survival of the virus and its capacity to multiply. A solution of soap (2%), and "Tego 103S" (an amphoteric surface-active agent) 2% had no apparent effect on either of the 2 viruses. Mercury perchloride 1% had a strong, and Zephyrol 2% and Riseptin 2% (quaternary ammonium compounds) a moderate, inactivating effect on influenza A virus but very little on Newcastle disease virus. Both

viruses were completely inactivated by chloramine 0·5% and Optal 30%, and almost completely by Havisol 2% (a phenolic of undisclosed composition). The action of Optal, which is apparently simply *n*-propylalcohol, impresses the author most, particularly because ethyl and methyl alcohol are said to have little virucidal effect.

L. P. Garrod

McLeod, Joyce A. & McLeod, J. W. **Oscillation of the Intraleucocytic Granules as a Criterion of Survival of the Leucocyte and of the Potency of Cytotoxic Agents.** *J. Path. & Bact.* 1959, Jan., v. 77, No. 1, 219–30, 1 fig. [21 refs.]

When leucocytes were suspended in 0·2–0·4% NaCl, oscillation of the intracellular granules took place. The appearance of the cells and the effect of temperature, time, suspending fluid and *p*H on the oscillation showed that it took place only in living cells and that substances which destroyed oscillation were lethal to the cells. The authors then used this criterion to study the cytotoxicity of a number of substances including antiseptics, quaternary ammonium compounds, sulphonamides and antibiotics. With the exception of formaldehyde, the phenylmethane dyes were the most toxic of the substances tested; and the antibiotics and weak antiseptics such as boric acid were the least toxic. The ratio was calculated between the highest concentration tolerated by leucocytes and the lowest concentration bactericidal for *Staphylococcus aureus, Escherichia coli* and *Pseudomonas pyocyanea,* tests being carried out in the presence of organic debris as well as in nutrient broth. Few substances tested in this way seemed likely to give favourable results when used to treat infected surfaces where there would be much protein debris. Apart from the antibiotics, chlorhexidine (Hibitane) appeared to be the best followed by mercurochrome and proflavine. *Sheila McDonald*

INDIVIDUAL BACTERIA

In this section the abstracts are arranged as far as possible in the following order: General; Enteric Organisms: Corynebacterium, Mycobacterium; Staphylococcus; Streptococcus; Brucella; Haemophilus; Pasteurella; Pseudomonas; Neisseria; Donovania; Spirochaetes; Leptospira; Anaerobes; Bacillus; Others.

Falkow, S. **Activity of Lysine Decarboxylase as an Aid in the Identification of Salmonellae and Shigellae.** *Amer. J. Clin. Path.* 1958, June, v. 29, No. 6, 598–600.

A simplified method for the detection of lysine decarboxylase is described. The medium consists of peptone (Bacto) 0·5%, yeast extract (Bacto) 0·3%, glucose 0·1% and L-lysine (Difco) 0·5%. Brom-cresol-purple is added and the medium distributed in 5 ml. volumes in screw-capped bottles and autoclaved.

Organisms of the Enterobacteriaceae ferment glucose with the production of acid which turns the medium from purple to yellow after 10–12 hours' incubation at 37°C. Those which produce lysine decarboxylase then form cadaverine and the medium reverts to the alkaline purple colour within 24 hours.

Read at 24 hours a purple colour is indicative of the strains positive for lysine decarboxylase—*Salmonella* and *Arizona*—and a yellow colour the negative strains—*Shigella,* Bethesda-Ballerup, *Proteus* and Providence. Variable results are given by *Escherichia* and *Klebsiella*—usually positive—and the Alkalescens-Dispar group. *J. Nagington*

McKinney, R. E.; Langley, H. E.; Tomlinson, H. D.; Campbell, H. **Survival of *Salmonella typhosa* during Anaerobic Digestion. I. Experimental Methods and High-Rate Digester Studies** [McKinney, Langley & Tomlinson]. *Sewage & Indust. Wastes.* Wash. 1958, Dec., v. 30, No. 12, 1469–77. **II. The Mechanism of Survival** [Langley, McKinney & Campbell]. *Ibid.,* 1959, Jan., v. 31, No. 1, 23–32, 11 figs. [11 refs.]

The economic advantage to be gained by the use of high-rate sewage sludge digestion, where the retention time can be reduced to as little as 6 days, is obvious but before such a modification of the established method can be accepted as safe, from a public health point of view, it is necessary to show that the much reduced retention period does not favour increased survival of pathogenic organisms.

The first of these 2 papers is concerned with the development of experimental methods that would give reproducible results of viable counts of various enteric bacteria, particularly *Salmonella typhi,* for the estimation of survival rates of these organisms when artificially infected sludge is exposed to anaerobic digestion under different conditions. The " spot-plate " technique, which appears to be similar to the Miles and Misra method, was used for viable counts with a variety of differential media—eosin-methylene-blue (EMB) was the medium of choice for *Escherichia coli, Aerobacter aerogenes* and Wilson and Blair's bismuth sulphite medium (BS) for *Salm. typhi.* It was found that the addition of large quantities of *A. aerogenes, E. coli* and *Salm. typhi* to digesters containing sterile raw sludge with variable retention periods resulted in a rapid " die-off " of the typhoid organisms. The continuous addition of *Salm. typhi* to 6-day and 20-day digesters showed a greater survival in the digesters with the shorter retention period.

The second paper examines the mechanism of survival of *Salm. typhi.* The most important finding was that, although the raw sewage sludge proved to be an adequate source of food for pure cultures of *Salm. typhi,* when this organism was inoculated into sludge with mixtures of *E. coli, A. aerogenes* and *Pseudomonas fluorescens* the latter organisms were much more successful than *Salm. typhi* in the competition for essential food stuffs. *Salm. typhi* requires high concentrations of tryptophan for survival and multiplication; this amino-acid is synthesized by *Salm. typhi* in

amounts inadequate for growth and the organism therefore depends on the availability of this essential material in the medium in which it is growing. It is sufficient in raw sludge to support the growth of *Salm. typhi* in pure culture, but in competition with the other enteric organisms, whose ability to synthesize tryptophan is in addition more adequate, the typhoid bacillus is unsuccessful. The concentration of available bacterial nutrient in a sludge digester decreases as the retention time is increased so that more tryptophan, with increased survival of *Salm. typhi* would be expected in the 6-day digester as compared with the 20-day digester. Even in long retention-period digesters some survival of *Salm. typhi* can occur and the authors conclude that the difference in health hazards between sludges from low-rate long retention and high-rate short retention digesters would be insignificant. *H. J. Bensted*

MUSCHEL, L. H., CAREY, W. F. & BARON, L. S. **Formation of Bacterial Protoplasts by Serum Components.** *J. Immunology.* 1959, Jan., v. 82, No. 1, 38–42. [27 refs.]

"Normal mammalian serum plus stabilizing agents effected conversion of the viable bacterial rods of *Escherichia coli* B and *Salmonella typhosa* Mrs. S., both rough organisms, into spherical protoplasts. A smooth organism, *S. typhosa* H901, was refractory, however, to the formation of protoplasts by normal serum, but addition of antiserum, complement, and lysozyme led to the formation of stabilized protoplasts of this organism. These protoplasts may conceivably play a role in the persistence of microbes in the animal body."

SPICER, C. C. & DATTA, Naomi. **Reversion of Transduced Antigenic Characters in** *Salmonella typhimurium.* *J. General Microbiol.* 1959, Feb., v. 20, No. 1, 136–43.

The results of transduction by bacteriophage of antigenic characters in the salmonella group, whereby the flagellar antigens are transferred between certain members of the group, have been assumed to represent a complete replacement of the genetic factor controlling the H antigen by the transduced gene. Many careful examinations of these synthesized cultures have been made to find any sign of the continued presence of the recipient's original H antigen. No sign was found; the synthetic types prepared by transduction appeared to be as stable as naturally occurring salmonella organisms. As far as is known this important paper records the first example of reversion of transduced antigenic characters.

The original observations were made on a synthetic culture (SL 150) which had been prepared some 3 years previously from a strain of *Salmonella typhi-murium* by 2 successive transductions with a bacteriophage (phage P22) lysate of *Salm. abony*; the H antigens had thus been altered from *i*<–>1·2 to *b*<–>*enx*. The particular culture of SL 150, on Dorset egg medium, had been stored in the dark at room temperature for a year before examination and was being re-investigated for another purpose by serum-selection procedures using heavy inocula on semi-solid agar containing antiserum to H antigen factors *b* and *enx*. A number of swarms developed from this culture which, on further investigation, were found to have the antigenic formula: 4,5,12; *i*<–>*enx*, and to be streptomycin- and azide-resistant. No such organism had ever been known in the laboratory and, as the possibility of contamination was ruled out, the new type was taken to be a reversion to the original 1st phase H antigen. Several earlier strains, from which this particular culture (SL 150) had been derived, were similarly examined and some were also found to contain a small proportion of *i*<–>*enx* forms. Single colony cultures with *b*<–>*enx*, as the H antigens were selected from some of these and stored on Dorest egg slopes at room temperature and at 4°C. for examination later.

In addition, a fresh series of transductions and selections was made, starting from the original strain of *Salm. typhi-murium*, from which the synthetic strain (SL 150) had first been prepared. These cultures differed from the previous series in being lysogenic for phage P22; neither SL 150 nor its relatives in that series carried phage P22—an important difference.

Some 8 months later a detailed study was begun of all the available cultures, from the authors' collection and additional sources, of SL 150 and related strains, including the single colony cultures referred to above and also the specially prepared series of cultures lysogenic for P22. None of the lysogenic cultures showed any evidence of reversion whereas with the various non-lysogenic cultures of SL 150 and its relatives, which were examined at that time, reversion was evident; the organisms had the H antigens either *i*<–>*enx* or *b*<–>1·2., but reversions in both phases were not detected.

These findings were fully confirmed in further studies related to this particular strain. Many other non-lysogenic salmonella strains, with H antigens altered by transduction, were examined for evidence of reversion, but in none was there any indication of antigenic instability.

There seems to be no satisfactory explanation of these most interesting and important observations at present. The work continues and various intriguing possibilities present themselves, but, since no method has yet been devised to control this reversion, progress may well be slow. *H. J. Bensted*

FURNESS, G. **Interaction between** *Salmonella typhimurium* **and Phagocytic Cells in Cell Culture.** *J. Infect. Dis.* 1958, Nov.–Dec., v. 103, No. 3, 272–7. [20 refs.]

Extensive studies of strains of *Salmonella typhimurium* of different mouse virulence have failed to disclose conclusive evidence of differences in their resistance to the body defences of the mouse. Previous work by this author [FURNESS & ROWLEY, this *Bulletin*, 1957, v. 32, 76; Furness, *Federation Proc.*, 1958, v. 17, 511] has indicated that mouse-avirulent strains of *Salm. typhi-murium* are more susceptible to

the action of macrophages in the peritoneal cavity of the mouse than virulent strains so that when such mixtures are injected intraperitoneally the avirulent tends to be eliminated while the virulent strain survives and multiplies. It was also found that cell cultures derived from monkey kidney tissue culture eliminated an avirulent mutant of *Salm. typhi-murium* from a culture whereas similar cell cultures were ineffective against the virulent strain. The present paper compares the effect on the highly virulent strains C5 and LT 2 and the avirulent strain M206 of the cell cultures of the altered monkey kidney cells and cell cultures of mouse macrophages.

It was first shown with both kidney cell and macrophage cultures that the virulent and avirulent strains were phagocytosed almost equally. There was a slight increase in the percentage of the virulent strain phagocytosed over the non-virulent strain by both cell cultures. On the other hand the bactericidal effect of the altered monkey kidney cell culture on the avirulent strain was very striking. In every experiment the majority of the avirulent organisms were killed off within 3 hours after which the viable count remained at this very low level for the following 12 hours whereas the virulent strains invariably survived and the viable counts rose significantly. Mouse macrophage cultures at first killed both virulent and avirulent organisms but after about 3 hours the former began to multiply whereas the viable counts of the avirulent remained at a very low level. In the case of the altered kidney cell cultures viable virulent organisms were appearing in the supernatant in 5–6 hours; with the mouse macrophage cultures this was postponed to about 9 hours, indicating that the cells were undergoing lysis. It is concluded that the ability of an organism to multiply in the mononuclear cells of its host is an indication of its virulence in respect of that host. *H. J. Bensted*

SCHEWE, Elenore. **Effects of Modified Host Metabolism and Altered Defence Mechanisms on Survival Time and Pathogen Counts in Tissues and Total Body of Mice infected intravenously with** *Salmonella typhimurium*. *J. Infect. Dis.* 1958, May–June, v. 102, No. 3, 275–93, 3 figs. [20 refs.]

Mice injected with a lethal intravenous dose of *Salmonella typhi-murium* died 46–150 hours later. The total viable count of this organism per animal at death was consistently 10^9–10^{10} bacteria.

Mice infected and then injected at intervals with disodium malonate either died within the next 12 hours from a toxic effect and had a low bacterial population similar to living control animals at this time or they died soon afterwards with the high bacterial population associated with moribund control animals.

These results are attributed to the cumulative action of the malonate and the bacterial endotoxin to cause the early deaths. The inhibition of the host tricarboxylic acid cycle by the malonate which produces a nutrient environment permitting a more rapid multiplication of the bacteria up to the lethal point is thought to be the reason for the later deaths.

A similar reduction in host survival time with increased bacterial multiplication to the usual lethal population was produced by injections of sodium monofluoroacetate. This is also an inhibitor of the tricarboxylic acid cycle by its action on the enzyme aconitase. [See also BERRY *et al.*, this *Bulletin*, 1956, v. 31, 1039.] *J. Nagington*

USHIBA, D., HIGUCHI, S. & OHASHI, T. **Relationship between** *in vitro* **Sensitivity to a Tissue Polypeptide and Virulence for Mice of** *Salmonella enteritidis*. *Keio J. of Med.* Tokyo. 1958, Nov., v. 7, 1–15, 2 figs.

KAUFFMANN, F. **On the Biochemical Behaviour of New** *Salmonella* **Types.** *Acta Path. et Microb. Scandinavica.* 1958, v. 43, No. 2, 175–84.

The biochemical reactions of the new salmonella serotypes described since the publication of the 2nd edition of the author's book on the Enterobacteriaceae in 1954 [this *Bulletin*, 1955, v. 30, 1036] are presented in tabular form.

The strains which give atypical reactions include Salmonella Fulica, which did not produce gas from glucose and mannitol and was ammonium-citrate-negative; Salm. Ahuza, Salm. Clifton and Salm. Mundonobo which fermented sorbitol after 2 days and Salm. Chinovum which did not ferment maltose.

Salicin was fermented by Salm. Jaffna and one culture of Salm. Ajiobo after 1 day and by Salm. Strasbourg, Salm. Mjimwema, Salm. Germiston and Salm. Boksburg after 2–6 days.

Salm. Ahuza, Salm. Chinovum, Salm. Ezra, Salm. Lisboa, Salm. Portland and Salm. Victoria were all "ammonium-weak", *i.e.* gave a negative or delayed positive reaction in ammonium-glucose and ammonium-citrate. *J. Nagington*

VAN OYE, E., LUCASSE, C., HERIN, V. & BEAUFORT, M. Trois nouveaux sérotypes du groupe *Salmonella* isolés au Congo Belge: *S. inganda* (6,7 : z10 : 1,5), *S. ipeko* (9,12 : c : 1,6) et *S. bolombo* (3,10 : z38 : –). [**Three New** *Salmonella* **Serotypes from the Belgian Congo: Salm. Inganda, Salm. Iseko and Salm. Bolombo**] *Ann. Inst. Pasteur.* 1959, Mar., v. 96, No. 3, 368–70.

The English summary appended to the paper is as follows:—

"Three new *Salmonella* serotypes isolated in the Belgian Congo are described, namely *S. inganda* (6,7 : z_{10} : 1,5), *S. ipeko* (9,12 : *c* : 1,6) and *S. bolombo* (3,10 : z_{38} : –)."

VAN OYE, E., VASSILIADIS, P., JANSSEN, P. & VAN LOOY, G. Une nouvelle *Salmonella* isolée au Congo Belge: *S. bukavu* (1,40 : L,z28 :1,5). [**A New** *Salmonella* **Isolated in the Belgian Congo: Salm. Bukavu**] *Ann. Inst. Pasteur.* 1959, Mar., v. 96, No. 3, 370–72.

The English summary appended to the paper is as follows:—

"The description is given of a new *Salmonella* serotype isolated from a native woman of the Belgian Congo: *S. bukavu* = 1,40 : $1,z_{28}$: 1,5."

LEVI, Eva & ZDRAVKOVIC, A. **Detection of *Shigella* on Different Vehicles which spread Bacillary Dysentery and the use of a Comparative Method for Isolation of Bacteria of the Intestinal Group from Sewage and River Water.** *Bull. Inst. Hyg.* Belgrade. 1958, v. 7, No. 2, 1–16, 2 figs. [15 refs.] [In Serbian.] English summary.

In an epidemiological investigation of a locality in Serbia persistently affected by bacillary dysentery attempts were made to isolate *Shigella* spp. from washings of the hands of the inhabitants, from flies and samples of earth collected in the vicinity of privies and from the water of wells. *Sh. sonnei* was found on the hands of 1 of 19 persons examined, and the same organism was isolated from stool specimens from 4 of the 9 members of his family, all of whom had previously suffered from a disease resembling dysentery. *Sh. sonnei* and *Sh. flexneri* 3 were each isolated in 1 instance from 55 flies. *Sh. boydii* 5, *Sh. sonnei* and *Sh. flexneri* 6 var. Manchester were isolated from the samples of well water. *D. J. Bauer*

ERLANDSON, A. L., Jr. & MACKEY, W. H. **Nutrition of *Shigella*: Growth of *Shigella flexneri* in a Simple Chemically Defined Medium.** *J. Bacteriology.* 1958, Mar., v. 75, No. 3, 253–7, 2 figs.

In an attempt to see if a simple nitrogen compound could provide the sole source of nitrogen, a chemically defined medium for the growth of *Shigella flexneri* was evolved which consisted of mineral salts, *i.e.* NaCl 0·85%, $MgSO_4,7H_2O$ 0·05%, K_2HPO_4 0·067 M. and KH_2PO_4 0·067 M.; 2 accessory growth factors—thiamin hydrochloride 0·03% and niacin 0·001%; a single carbohydrate energy source—glucose 1·0%; and a single amino acid nitrogen source—L-aspartic acid 0·25%.

Although some inorganic ammonium compounds and amino acids could also serve as the sole nitrogen source the maximum growth was obtainable only with aspartic acid. Only the natural isomer, L-aspartic acid, was utilizable and there was no evidence of its inhibition by the D-isomer. *J. Nagington*

OKADA, S., SAKAKI, T. & KARATO, T. **Antigenic Variations in *Shigella flexneri* 1b, 3 and 4 b.** *Japanese J. Microbiol.* 1958, July, v. 2, No. 3, 271–8. 1 fig. [14 refs.]

Natural variation in the antigenic make-up of the Flexner dysentery organisms, due to loss of the specific type antigen with an apparent increase of the group factors, is not an uncommon phenomenon and occasionally this loss may involve the group antigens. This paper is concerned with the demonstration of the antigenic instability of certain Flexner strains by the selective action of appropriate antisera. For instance, when *Shigella flexneri* 1 a (I,4) is cultivated in broth containing pure type I serum it is possible to recover from plate cultures organisms that possess only the group-factor 4. Although the authors call this induced variation it would appear to be due to selection by the serum on cultures which already contain small numbers of the variant.

When, however, *Sh. flexneri* 1 b was grown in broth containing pure type I serum, cultures were recovered that had the antigenic characters of *Sh. flexneri* 3. Likewise when *Sh. flexneri* 4 b was cultured in broth containing pure type IV serum it was also possible to obtain from plate cultures *Sh. flexneri* 3. The possession of group-factor 6 by both strains 1 b and 4 b was found to be an indispensable condition for the demonstration of this variation. In this connexion it will be recalled that earlier work, at any rate with regard to *Sh. flexneri* 1 b (VZ), had shown a peculiar antigenic structure and that some strains appeared to be very closely related to type Z (3) and the authors' suggestion that the association of type III antigen and group-antigen factor 6 is so close that they could be regarded as 2 components of a single antigen molecule seems more reasonable than the alternative suggestion that involves antigen synthesis. In the experiments reported in this paper type III and group 6 antigens never underwent loss or variation independently of each other and only one natural variant containing group antigen 6 but lacking type III antigen has been reported by EWING [this *Bulletin*, 1954, v. 29 (987); *J. Immunology*, 1954, v. 72, 404]. *H. J. Bensted*

ERLANDSON, A. L., Jr., LAMPLEY, E. L. & FLOYD, T. M. **Experimental *Shigella flexneri* Infections in Chick Embryos.** *J. Infect. Dis.* 1958, May–June, v. 102, No. 3, 237–42, 1 fig.

The LD50 of a *Shigella flexneri* 3 strain was 10^7 organisms when inoculated into the allantoic fluids of chick embryos 8 days old. The embryos which died had a generalized infection and superficial lesions which ranged from small septic foci to massive haemorrhage. Those which survived and were allowed to hatch were found to have shigellae on the skin and a bacteraemia which persisted for 24–36 hours after hatching. They excreted a pure *Sh. flexneri* flora for 24–36 hours after which the normal gut organisms began to appear and after 6 days these had completely replaced the shigellae.

Infected embryos were used to study the antibacterial action of a series of antibiotics and other drugs. Only 3 were toxic to the embryos—tetracycline, tyrothricin and "triple sulfa", *i.e.* a mixture of sulphadiazine, sulphamerazine and sulphamethazine. Chloramphenicol, dihydrostreptomycin and polymyxin B were alone able to give complete protection. Almost complete protection was afforded by gantrisin, neomycin and oxytetracycline. A dose of 25 mgm. gantrisin was protective only if inoculated within a short time of the bacteria—given 2 hours after the bacteria it was almost without effect. Chloramphenicol was capable of giving complete protection when 50 μgm. or more was given as late as 4 hours after the bacteria. *J. Nagington*

SERÉNY, B. **Aetiotropic Treatment of Experimental Shigellosis.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 2, 79–91, 2 figs. [17 refs.]

Experimental keratoconjunctivitis was produced in 250 guineapigs by conjunctival infection with shigella

strains and it was treated with several "aetiotropic agents", *i.e.* chloramphenicol, oxytetracycline, streptomycin, sulphamethizole, and sulphaguanidine. Altogether 300 such treatments were carried out, mostly by local application into the palpebral fissure with a smaller series of oral and intramuscular administrations.

It was found that in the majority of infections there was a good therapeutic response but there was an unexpectedly high proportion of failures. For example, about 2/3 of 236 infections treated locally with chloramphenicol recovered within 1 week of the start of treatment but the rest recovered only slowly or became chronic.

Poor therapeutic response could be caused by an inadequate concentration of the drug at the site of infection, too short a period of treatment and resistance of the strains used, but it is felt that a weakness in the defence mechanisms of the host is probably more important. *J. Nagington*

HARRIS, T. N., HARRIS, Susanna & TULSKY, E. **Studies on the Transfer of Lymph Node Cells. XIII. Effect of X-Irradiation on Lymph Node Cells incubated *in vitro* with *Shigella*-Trypsin Filtrate.** *J. Immunology.* 1959, Jan., v. 82, No. 1, 26–31, 2 figs.

ANDO, K., TADOKORO, I. & YAMASHITA, A. **Studies on the Dysentery Chrome Vaccine. Methods of its Preparation and Field Trials.** *Japanese J. Exper. Med.* 1958, Oct., v. 28, No. 5, 353–74. [20 refs.]

The work described in this paper is related to the claim that the treatment of some bacillary suspensions with chromium salts stabilizes and preserves their antigenic structure (including the surface antigens), thus preventing loss of antigenicity, and at the same time reduces their toxicity when such killed suspensions are injected into man or animals.

In investigating the protective value of bacillary dysentery vaccines the authors prepared a vaccine against *Shigella flexneri* 2 b by taking a freshly made thick suspension of this organism in 1% formalin and adding to it an equal volume of a mixture containing equal parts of a solution of chrome alum (0·4%) and a solution of sodium thiosulphate (0·4%). This was incubated at 22°C. for 5 days with frequent shaking, then, after centrifugation and 3 washings in 0·5% formol-saline to remove any unbound chromium, the bacterial cells were re-suspended in fresh saline in a concentration of 100 mgm./ml.

Tested in mice, guineapigs and rabbits the preparation was found to be significantly less toxic than formolized or heat killed vaccines and, judged by the antibody response, the antigenicity was considerably enhanced when injected into these animals and human beings. In trials with a solid form of vaccine given orally after previous intracutaneous vaccination the development of both copro- and serum-antibodies was noted. The assessment of the protective value of such a specific bacterial vaccine against bacillary dysentery is a formidable undertaking and the fact that the results were inconclusive was not unexpected. *H. J. Bensted*

KELEN, A. E. **Production of OB Diagnostic Antisera from Motile *Escherichia coli* Strains.** *Canadian J. Microbiol.* Ottawa. 1958, Dec., v. 4, No. 6, 581–91. [14 refs.]

Diagnostic OB antisera for the *E. coli* group are usually prepared from live strains, without any particular effort to suppress H antigenicity; thus, unless the immunizing strains are non-motile, flagellar agglutinins will be present in many OB sera. The present paper describes how non-motile "variants" of motile *E. coli* strains may be produced by growth on agar plates containing 0·1% phenol, and thereafter used as immunizing antigens to produce OB antisera containing no demonstrable H agglutinins. *E. coli* O125 and O126 were used in the experiment: they were made highly motile by Craigie tube passage, grown in broth containing the homologous H antiserum (this step may be omitted), and then plated out on the phenolized agar. At this stage the organisms were tested with OB and H antisera, and if the H component was still in evidence, further plating on phenolized agar was indicated. Immunization of rabbits was carried out in the usual way; the resulting antisera gave satisfactory O and B titres and were shown to contain no H agglutinins. *John S. Stevenson*

HYLIN, J. W., FIEDLER, Hildegarde & WOOD, J. L. **Thiocyanate Formation by Extracts of *Escherichia coli* and of Liver.** *Proc. Soc. Exper. Biol. & Med.* 1959, Jan., v. 100, No. 1, 165–8, 3 figs. [10 refs.]

JONSEN, J., LALAND, S. & STRAND, Å **Degradation of Deoxyribose by *E. coli*. Studies with Cell-Free Extract and Isolation of 2-Deoxy-D-Ribose 5-Phosphate.** *Biochim. et Biophys. Acta.* 1959, Mar., v. 32, No. 1, 117–23, 1 fig. [13 refs.]

LOEB, Marilyn R. & COHEN, S. S. **The Origin of Purine and Pyrimidine Deoxyribose in *Escherichia coli* Systems.** *J. Biol. Chem.* 1959, Feb., v. 234, No 2, 360–63. [25 refs.]

GORINI, L. Regulation en retour (Feedback Control) de la synthèse de l'arginine chez *Escherichia coli*. [**Feedback Control of Arginine Synthesis in *Escherichia coli***] *Bull. Soc. Chimie Biol.* 1958, v. 40, No. 12, 1939–52, 1 fig. [24 refs.]

NISMAN, B. **Incorporation and Activation of Amino Acids by Disrupted Propoplasts of *Escherichia coli*.** *Biochim. et Biophys. Acta.* 1959, Mar., v. 32, No. 1, 18–31, 10 figs. [26 refs.]

SARKAR, J. K., CHOUDHURY, B. & TRIBEDI, B. P. ***Alcaligenes faecalis*—its Systematic Study.** *Indian J. Med. Res.* 1959, Jan., v. 47, No. 1, 1–12, 4 figs. on pl. & 1 graph. [29 refs.]

This is a report on the morphological, cultural, biochemical, antigenic and pathogenic characters of 200 strains of *Alcaligenes faecalis* [*Bact. alkaligenes*] isolated

from the blood, cerebrospinal fluid, pus, urine, pleural and peritoneal exudates of patients suffering from a variety of conditions. A report on the examinations for pathogenicity on the same series of strains has already been published [this *Bulletin*, 1959, v. 34, 482]. The authors were able to define 5 distinct morphological types in the 200 strains: coccal (9), coccobacillary (38), rods (125), filamentous (8) and vibrio (20). It is difficult, from the account given, to relate special characters to particular strains but there were 30 strains with a single polar flagellum, 64 with peritrichate flagella and 57 non-motile non-flagellated strains. Some of the strains showed some tendency to retain Gram's stain and there were unimportant differences in biochemical reactions. Antigenic relationship between the strains could not be established.

[This is an incomplete study; the results are in general agreement with previous published work on this subject (NYBERG, C., *ibid.*, 1935, v. 10, 413), but they do not provide information of much greater value. In spite of the fact that the 20 vibrio forms were all isolated from patients convalescent from cholera the authors do not favour these being classified as *Vibrio alkaligenes*, as Nyberg would have probably suggested, but prefer to regard the whole group as constituting a special division of organisms in accordance with the Bergey system—*Alcaligenes faecalis*.]

H. J. Bensted

SHNEERSON, A. N. **Study of the Toxigenicity of Newly Isolated Strains of Diphtheria Bacillus by Precipitation of Toxin in Phosphate-Peptone Agar.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 11/12, 1719–23. [Translated from Russian.]

For the detection of lines of precipitation of toxin and antibody in gel diffusion plates, the author has found it possible to substitute a phosphate peptone agar for the meat-extract peptone agar reinforced with serum which is commonly used. In preparing this medium, 40 gm. of dried agar, 7·125 gm. of disodium phosphate and 3·75 gm. of potassium dihydrogen phosphate are added to a litre of distilled water and dissolved in an autoclave with flowing steam. Equal volumes of this and of an extract of minced pig's stomach treated with 1% hydrochloric acid for 18–20 hours at 37°C., are used. 0·3% of maltose and 0·5% of sodium acetate are finally added to the medium.

This medium has been tried out by the author and, independently, by the Moscow Institute of Epidemiology and other institutes. These institutes report favourably on the medium, having used it for the investigation of 663 newly isolated strains of which 248 were shown to be toxigenic. Parallel determinations by lines of precipitation in gel diffusion plates in this medium on the one hand and by guineapig inoculation on the other showed 5 strains toxigenic *in vivo* but missed on the plates. 25 were negative *in vivo* but positive on the *in vitro* test. [There is a misprint in the table recording these observations—"*in vitro*" for "*in vivo*" in the last column.] A considerable proportion of the discrepancies in which a positive plate test corresponded to a negative animal test is accounted for by the development of late and feeble lines of precipitation which are probably explained by bacterial antigens other than the specific toxin [this *Bulletin*, 1950, v. 25, 514, 636]. It is thought that lines which appear after 72 hours should not be taken into account. The difficulties introduced by the appearance of such lines are discussed.

Observations on the correlation between cultural type of the organism and toxigenicity are also given for 75 strains:

26 strains of *Corynebacterium diphtheriae* (*gravis* type)			—all toxigenic.
32	,, ,, ,, ,,	(*mitis* ,,)	—25 toxigenic.
8	,, ,, ,, ,,	(atypical)	— 5 toxigenic.
8	,, ,, *C. hofmanni*	...	—non-toxigenic.
1	,, ,, diphtheroid (unspecified)	...	—non-toxigenic.

J. W. McLeod

GUREVITCH, J., WEBER, D. & IZAK, G. **The Syrian Hamster as an Experimental Animal in the Diagnosis of Tuberculosis.** *Bull. Res. Counc. of Israel.* 1958, Oct., v. 7E, No. 3, 182–8.

The authors, writing from Jerusalem, have been stimulated by the difficulties of obtaining a constant supply of guineapigs to reinvestigate the use of Syrian hamsters in the diagnosis of tuberculosis. They injected 2 groups of 4 hamsters with 5 million and 50 million tubercle bacilli, respectively, and 2 more groups of 4 hamsters were injected with the same numbers of bacilli, heated at 70°C. for 1 hour, in order to study the tissue reactions.

The animals injected with the living bacilli died between the 57th and 80th day and showed gross evidence of tuberculosis. The lungs of 7 of the animals and the spleens of 3 contained scattered tubercles and smears of these organs showed tubercle bacilli; the eighth animal had widespread lesions. In 6 of the animals the histological picture was unusual, there being patchy thickening in the interalveolar septa, caused by an exudate containing large mononuclear cells which bore no resemblance to the epithelioid cells of the tubercles; these areas of interstitial pneumonia containing many acid-fast bacilli. None of these animals excreted tubercle bacilli in the urine.

The animals injected with the dead bacilli were killed on the 83rd day, and although they had been injected in the inguinal region, acid-fast bacilli were found in the lungs and spleens of 2 of them; viable tubercle bacilli were recovered from 1 of them. Consolidation of 1 or 2 lobes of the lungs was found in 4 animals and histological examination revealed interstitial pneumonia; tubercles were found in the spleen of 1 animal.

Guineapigs inoculated at the same time with living bacilli died within 14 to 30 days of typical tuberculosis: those which received the heated bacilli were largely negative, but cultures from the organs were positive in 2 [in the relevant table, the headings "Heated" and "Living" appear to have been transposed].

The conclusion is that although the guineapig is the animal of choice, the hamster can be used for diagnostic purposes but it should not be killed for 3 to 4 months after inoculation. *S. R. M. Bushby*

LEBEK, G. Über den Nachweis des unterschiedlichen Sauerstoffoptimums des humanen und bovinen Mykobacterium tuberculosis (Beitrag zur Typenbestimmung der säugetierpathogenen Tuberkelbakterien). [**The Demonstration of Different Optimal Oxygen Concentrations for Human and Bovine** *Mycobacterium tuberculosis*] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 7/8, 581–7, 1 fig. [15 refs.]

When a suitable and defined solid medium, that of Sauton, of *p*H 7·2 and reinforced with 10% of inactivated ox serum, is inoculated with 0·5 ml. of a fine suspension of *Myco. tuberculosis* per 4·5 ml. of medium it is possible to demonstrate a constant difference between recently isolated strains of human and bovine type. The human strains grow heavily at the surface and to a depth of 4–7 mm. The bovine strains show growth as a layer of opacity 1–2 mm. in depth and 12–20 mm. below the surface.

Clearness of the medium is essential and to this end the *p*H level of 7·2 is important nor should the temperature at which the ingredients are mixed exceed 50°C. The suspension used for inoculation should contain about 4 mgm. of bacteria per ml.

In all, 118 human strains (some drug resistant) and 94 bovine strains have been tested by this criterion and have given the results described. The only exceptions encountered have been 2 old laboratory strains, BCG and Ravenel, which, although bovine in origin, behaved like human strains when cultivated by the above method; but since they no longer comply with other recognized tests for bovine strains, this exception is not significant.

J. W. McLeod

MANKIEWICZ, Edith. **Agar Diffusion Precipitation and Complement Fixation Tests applied to the Study of the Antigenic Relationships between Chromogenic Acid-Fast Bacteria and** *Mycobacterium tuberculosis*. *Canadian J. Microbiol.* Ottawa. 1958, Dec., v. 4, No. 6, 565–70.

The chromogenic acid-fast bacteria examined by these serological methods were 42 strains from among 1,060 positive cultures from pathological specimens examined in 1955–6 and 24 of the patients from whom these organisms were isolated had yielded cultures of typical tubercle bacilli on one or more occasions.

For the agar diffusion studies antisera were prepared by injecting rabbits with heat-killed suspensions of *Mycobacterium phlei*, BCG, H37Rv and 2 of the chromogenic acid-fast bacilli and these were tested in Petri dishes against lipid antigens extracted from the 42 strains, *Myco. phlei*, BCG, H37Rv and 3 strains of recently isolated tubercle bacilli by shaking with a mixture of ethanol ether and hydrochloric acid. The 2 strains of chromogenic acid-fast bacilli were selected because one had produced a progressive disease and the other a retrogressive disease in guineapigs. From the number and the position of the lines of precipitation, the chromogenic bacilli were roughly classified into 3 groups: I those related to the pathogenic tubercle bacilli; II those related to the saprophytes; III those related to both pathogenic tubercle bacilli and the saprophytes; and IV those related to neither of these bacilli. Only the chromogenic bacilli of group I produced progressive disease and, whereas all guineapigs injected with group II became tuberculin-positive, only some of those injected with III or IV became positive.

These antigens and antisera were used in the complement-fixation tests and the results showed the same overlapping between typical and atypical tubercle bacilli on the one hand and the saprophytes on the other; this test, however, enabled quantitative differences to be detected between the individual strains.

S. R. M. Bushby

ASSELINEAU, J., BUC, H., JOLLÈS, P. & LEDERER, E. Sur la structure chimique d'une fraction peptidoglycolipidique ("cire D") isolée de *Mycobacterium tuberculosis* var. *hominis*. [**Chemical Structure of a Peptide-Glycolipid Fraction Isolated from** *Mycobacterium tuberculosis* **(Human Strain)**] *Bull. Soc. Chimie Biol.* 1958, v. 40, No. 12, 1953–64, 2 figs. [40 refs.]

TAKAHASHI, Y. & ONO, K. Modification par chauffage du pouvoir hémo-sensibilisant des antigènes polyosidiques issus de la tuberculine. [**Modification by Heating of the ability of Tuberculo-Polysaccharides to Sensitize Red Cells**] *C.R. Soc. Biol.* 1958, v. 152, Nos. 8/9, 1301–3.

That different samples of the tuberculin antigens vary in their ability to sensitize red cells for the agglutination test is well recognized. In this paper the authors show that when heat sterilization of the original culture of tubercle bacilli by autoclaving at 120°C. for 30 minutes was avoided by using filtration and the resulting tuberculin was concentrated at a temperature below 40°C., the tuberculo-polysaccharide isolated by deproteinization and precipitation with methanol sensitized red cells for agglutination at a titre of 640 whereas the polysaccharide derived from heat-killed culture was inert. The heating, however, did not affect the ability of the polysaccharide to act as a precipitinogen or a neutralizing antigen.

The extent of the deleterious effect on agglutination was shown to depend partly upon the *p*H of the solution; heating the polysaccharide at *p*H 4·0 caused a smaller loss in the haemagglutination titre than heating at *p*H 7·0, and heating at *p*H 10 completely abolished the sensitizing power of the antigen although its precipitating and neutralizing properties were still intact.

S. R. M. Bushby

ARIMA, J., YAMAMOTO, K., MORIKAWA, K. & TAKAHASHI, Y. Sur le développement tardif de l'allergie tuberculeuse chez le Cobaye à la suite de l'inoculation intraveineuse du BCG. [**Delayed Development of Tuberculin Allergy in Guineapigs after Intravenous Inoculation of BCG**] *C.R. Soc. Biol.* 1958, v. 152, Nos. 8/9, 1292–5, 2 figs.

In a previous communication [in Japanese] the authors had reported that the development of tuberculosis in the guineapig from the subcutaneous injection of virulent tubercle bacilli was suppressed by the simultaneous injection of a large dose of BCG. In the present report they show that the intravenous injection of 10 mgm.

of BCG, 1 to 7 days after infection with virulent tubercle bacilli delayed the development of a positive reaction to tuberculin for about 3 weeks and that a delay was observed with a dose of BCG as low as 0·1 mgm. but not with 0·01 mgm. A similar delay was produced by H37Ra and killed virulent tubercle bacilli but not by avian tubercle bacilli. *S. R. M. Bushby*

SIGNORINI, L. F., MASSONE, F. & GRILLI, M. R. Ulteriori ricerche sperimentali sull'efficacia protettiva della anatubercolina integrale Petragnani, anche in confronto col BCG. Influenza della ripetizione dello stimolo vaccinale. [**Further Experimental Studies on the Protective Action of Petragnani's Complete Anatuberculin, including Comparisons with BCG. Effect of Repeated Vaccinal Stimulus**] *L'Igiene Moderna.* 1958, July–Aug., v. 51, Nos. 7/8, 559–83. [93 refs.] English summary.

This investigation was prompted by the conflicting views on the value of killed vaccines, and especially to study the effects of a repetition of the vaccinal stimulus; the average time of survival after infection, allergy changes and the presence of circulating antibodies were used as indications of resistance.

Tests were done on 15 groups of guineapigs (there were 141 animals at the start), 5 groups of which received Petragnani's complete anatuberculin (*Anatubercolina Integrale Petragnani*, referred to as AIP), 5 received BCG, and 5 served as controls. One of each of the treated groups was vaccinated once, a second group twice, a third group thrice and so on, with an interval of 30 days between treatments. Vaccination was done by a multipuncture intradermal method. BCG was used at a concentration of 20 mgm. (moist weight) per ml. AIP was used in a concentrated form as issued by the Sclavo institute, at 600 mgm. per ml. Petragnani's diagnostic anatuberculin, in an intradermal injection of 0·1 ml., was used to detect allergic change; reactions with a diameter greater than 3 mm. were taken as positive. The Middlebrook-Dubos haemagglutinin reaction was used at various intervals, with antigen IP 48 of the Pasteur Institute. The challenge dose was given 30 days after the last vaccination, by an injection of 1 mgm. (moist weight) of human *Mycobacterium tuberculosis*. The number of living bacteria used in each case ranged from 1 to 5 millions.

Except for the result after a single vaccination, the tuberculin reaction was, to a very small extent, more often positive in the BCG than in the AIP groups. After 2 vaccinations practically every animal reacted positively and subsequent changes were only small.

Haemagglutinin antibodies were sought in 4 animals which had received 3 and in 4 which had received 5 BCG and AIP vaccinal treatments respectively, their serum being examined before the beginning of treatment, 1 month after vaccination, and also 1 month and 3 months after being challenged, approximately equally positive results being obtained.

Survival time after infection in animals treated with BCG was longer than in controls to a statistically significant degree; in those treated with AIP this was only the case in animals which received 5 vaccinations. Repetition of the stimulus appears therefore to play a very important role in the killed vaccine, while it seems to improve results only to a limited extent in BCG.

The authors conclude that differences between live and killed vaccines were only quantitative.

E. Agius

CROWLE, A. J. **Immunizing Constituents of the Tubercle** *Bacillus. Bact. Reviews.* 1958, Sept., v. 22, No. 3, 183–203. [145 refs.]

In introducing this review the author reminds us that a moderately effective vaccine against tuberculosis was developed empirically some 40 years ago and that today this vaccine is still the best available, thus attesting to how little has been learned of the manner in which tuberculo-immunity is induced.

The tuberculo-polysaccharides have generally been shown to act as haptenes, but there have been 2 important exceptions. SEIBERT'S high molecular weight polysaccharide II has behaved as a definite antigen although its antigenicity may have been due to it being complexed with a lipid. TODA and MURATA (*Beitr. Klin. Tuberk.*, 1939, v. 93, 64) also described some important but unconfirmed experiments which demonstrated antigenicity in a polysaccharide isolated by precipitation with alcohol from tuberculin after the proteins had been removed by acidification and the polypeptides by adsorption on to kaolin.

Although the tuberculo-proteins derived from culture fluid or directly from the bacilli stimulate the production of antibodies and produce a state of allergy, there is conclusive evidence that they do not immunize against experimental tuberculosis.

The lipids represent as much as 40% of the dried weight of the tubercle bacillus and many investigations have been made with them. They have been shown to be responsible in part or entirely for many of the physical and biological properties of the bacillus, *i.e.* provocation of tuberculin allergy, immunologic adjuvant activity, induction of antibody formation, acid-fastness, hydrophobic characteristics and possibly virulence. The lipids have been classified by ANDERSON and by ASSELINEAU and others as acetone-soluble fats, phosphatides, waxes and "firmly bound" lipids, which can only be removed by such harsh treatment as hot acid or alkaline alcohol.

All the experiments with the acetone-soluble lipids show them to be non-immunizing—in fact, they appear to decrease resistance, but in contrast to these lipids, the phosphatides have frequently been shown to be therapeutic and prophylactic agents. The classical fractionation from ether-alcohol extracts provides purified phosphatide, but the phosphatide that has proved the most interesting is the one extracted by methanol from acetone-washed bacilli; this extract is the methylic antigen (*antigène méthylique*) and it has antituberculous activity *in vivo*. Although it is primarily a phosphatide, it contains fats, waxes and complex nitrogenous materials, and it may be that it is these non-phosphatides that are responsible for the antigenicity of the fraction, seeing that pure phosphatides are merely haptenic.

However, the antituberculous activity of methylic antigen may not be due to an ability to induce classical immunity. Evidence for this is that the protection it affords is not accompanied by tuberculin sensitivity, the protection lasts for only about 4 months, and it enhances the immunity of BCG. Moreover, very large quantities are necessary to give protection; quantities required are 10–100 times more than the minimum quantity of killed bacilli necessary to give classical immunity. The fact that this extract can bolster the immunity of the most effective known agent, *i.e.* BCG, certainly suggests that it has a different mode of action, and the stimulation of protective enzymes in the host, *e.g.* phosphatidase, or detoxification of irritating substances in the bacilli, have been suggested.

If tuberculophosphatide is responsible for the antituberculous activity of methylic antigen then phosphatides prepared by other methods should also be active. The evidence from a number of workers is, however, conflicting and its role at the moment must remain in doubt.

The waxes of the tubercle bacillus have been divided into 4 major fractions, A, B, C and D, and in spite of their being the subjects of many chemical and biological experiments, almost no attention has been given to their possible roles in immunity. The evidence available, however, suggests that neither C nor D is responsible for the immunity produced by the intract bacilli, and that A is probably inactive; the role of B is completely unknown.

A large number of investigations has been made on the effects of combined constituents and after reviewing the results, the author concludes that the failure of single pure preparations to induce immunity could be due to the need of more than one antigen to produce an effect. Paraffin oil extracts have immunized only when they have been known to contain lipids, polysaccharides and proteins; crude extracts of disrupted bacilli can be immunogenic and there are indications that their activity is due to mitochondria-like particles or, expressed chemically, to the combined activity of protein and lipid.

Finally, consideration is given to the capabilities of bacteria other than the tubercle bacillus to immunize against tuberculosis. Apart from other mycobacteria, a mixture of the typhoid bacillus and the gonococcus has afforded some protection but autolysates have been even more effective. The protection given by a concomitant infection with *Brucella abortus* in mice, however, appears to be due to the brucellae being intracellular and in some way increasing the resistance of the phagocytes to the tubercle bacillus.

S. R. M. Bushby

CONSTANTINESCO, N., HORNET, T., BIRZU, N., ZAVATE, O., PENCEA, I. & RUSAN, S. Rôle des bacilles tuberculeux tués dans la pathogénie de l'encéphalomyélite dite "allergique", provoquée par de l'extrait cérébral additionné avec des adjuvants de Freund. [**Role of Killed Tubercle Bacilli in the Pathogenesis of so-called "Allergic" Encephalomyelitis induced by Brain Extract plus Freund's Adjuvants**] *Ann. Inst. Pasteur.* 1959, Jan., v. 96, No. 1, 79–92, 10 figs. [18 refs.]

By injecting intramuscularly a suspension of sheep brain in Freund's adjuvant, encephalomyelitis was produced in 56 of 72 guineapigs, which suggests that the lesions were allergic in origin due to sensitization by the specific brain antibodies. However, the injection of Freund's adjuvant alone was followed by encephalomyelitis in 16 of 52 guineapigs. The adjuvant consists of lanolin, liquid paraffin and dead mycobacteria (in these experiments the latter were either virulent tubercle bacilli or BCG), and when the brain tissue + mycobacteria or brain tissue + lanolin + liquid paraffin were injected into groups of 37 and 11 animals, respectively, no animal developed brain damage. Thus mycobacteria plus the oil are apparently responsible for this damage and the presence of brain tissue increases its frequency.

The presence of widespread lesions characteristic of tuberculosis suggests that tuberculous allergy is the cause of the cerebral damage. These lesions were present in the meninges as well as the injection site, the glands, liver, spleen and lungs, and they were produced by the injection of adjuvant, with or without the brain tissue. Desensitization with tuberculin, however, had no effect on the incidence of the brain damage, and neither did daily injections of brain suspension aimed at desensitizing to this tissue; the injection of an antihistamine drug twice daily also had no effect on the damage.

The authors maintain that the results of their experiments do not support the hypothesis that the encephalomyelitis is of allergic origin.

S. R. M. Bushby

SUTER, E. & STRAIN, Anne K. **Infectivity and Immunogenicity of** *Mycobacterium X* **in Mice.** *Amer. Rev. Tuberculosis.* 1959, Jan., v. 79, No. 1, 47–51.

This mycobacterium was originally isolated from the brain of a mouse but there is evidence that it does not multiply in this animal, and that guineapigs, rabbits and chickens are completely resistant to it [*Amer. Rev. Tuberculosis,* 1955, v. 71, 88, 97]. There is also evidence which shows that tubercle bacilli do not multiply in monocytes derived from guineapigs which have been inoculated with it, so the authors have investigated the relationship between its behaviour in tissues and its immunogenic capacity.

In the first experiments, mice were infected intravenously with 9-day-old cultures of *Mycobacterium X* in Dubos medium and at intervals ranging from 1 to 89 days viable counts were made on the livers and spleens. The counts showed that for the first 7 days the number of bacilli remained constant and then slowly declined, indicating that no multiplication occurred. In a 9-day-old culture the bacilli are coccobacillary but there was no significant difference in the counts when the organisms were injected from a 2-day-old culture in which they are in a long bacillary form.

In further experiments, vaccination with *Myco. X* was shown to have a similar immunological effect to vaccination with BCG. The immunity was judged by the number of H37Rv present in the lungs of mice 35 days after challenge, made 41 days after vaccination,

or by the survival rate of mice challenged 4 weeks after vaccination. The vaccines contained approximately 10^7 BCG and 10^8 *Myco. X.* In another experiment the Vallée bovine strain was used as the challenge organism because it produces a more acute infection; the immunity afforded by *Myco. X* was again similar to that by BCG except when the vaccinating dose was reduced 100-fold, when BCG gave the better protection. In this experiment heat-killed bacilli were shown to be less effective than living ones. *S. R. M. Bushby*

COLWELL, Charlotte A. **Antimycobacterial Activity of Extracts of Rat Peritoneal Cells.** *Proc. Soc. Exper. Biol. & Med.* 1958, Dec., v. 99, No. 3, 662–5, 1 fig. [10 refs.]

The peritoneal cells used in these experiments were from rats and guineapigs, these animals being chosen because they represent the 2 extremes of natural resistance to the tubercle bacillus. The cells were obtained from exudates produced by the intraperitoneal injection of glycogen, and, after washing, the cells were disintegrated by 9 Kc sonic oscillation. To sterile filtrates of the extract, corresponding to 45–55 million cells per ml., suspensions of H37Rv were added and viable counts made at intervals up to 48 hours.

The result showed that whereas the suspension of H37Rv in the extract of the rat cells showed a drop from more than 250 to 2 or less viable units per 0·02 ml. during the 48 hours, there was no fall in those in the extract of guineapig cells and in distilled water.

Thus, the extract of cells from the animal highly resistant to the tubercle bacillus is tuberculocidal but that from the cells of a highly sensitive animal is apparently without effect on them. However, the cells from the guineapig were 90–95% macrophages and whereas those from the rat were similar, 4–6% of them were mast cells and their role was not determined.

S. R. M. Bushby

KOSMODAMIANSKY, V. N. & KLIMACHEVSKAYA, V. F. [**The Action of Soluble Saluzid on Tubercle Bacilli**] *Problemy Tuberkuloza.* 1959, v. 37, No. 1, 88–93. [In Russian.] French summary.

Saluzid is a derivative of isoniazid and was found to have a bacteriostatic action on tubercle bacilli to a dilution of 1 in 4,000,000 in Sauton medium. Resistance has been observed and the virulence of the resistant bacilli is considerably reduced. Guineapigs infected with 1 mgm. of these organisms do not lose weight, or die, and the infection runs a benign course without any tendency to spread. *Charles Wilcocks*

YAMAMOTO, T., NISHIURA, M., HARADA, N. & IMAEDA, T. **Electron Microscopy of** *Mycobacterium leprae murium* **in Ultra-Thin Sections of Murine Leprosy Lesions.** *Internat. J. Leprosy.* New Orleans. 1958, Apr.-June, v. 26, No. 2, 111–14, 5 figs. on 3 pls.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1959, v. 56, 630.]

OEDING, P. & WILLIAMS, R. E. O. **The Type Classification of** *Staphylococcus aureus*: **a Comparison of Phage-Typing with Serological Typing.** *J. Hygiene.* 1958, Dec., v. 56, No. 4, 445–54. [16 refs.]

The bacteriophage and serological methods of identifying types of *Staphylococcus aureus* were compared by typing by both methods 223 strains of coagulase positive staphylococci and also some groups of strains which were considered to have a common origin.

Tables are given which record the frequency distribution of serological types and phage-types among 239 and 750 independent strains respectively.

The results of the comparative typing showed that the 3 major groups of phage-types [this *Bulletin,* 1956, v. 31, 1037] corresponded broadly to the 4 groups defined among serotypes. A few serotypes were associated with particular phage-types but in general there was little correlation between the individual types recognized by the 2 techniques. However, consistent results in the recognition of related strains were obtained with either method.

A far greater number of types can be recognized by phage-typing but the proportion of untypable strains is higher than with serological typing. There is some variation in the types identified by both methods but this has been assessed more accurately in relation to phage-typing [*ibid.,* 1953, v. 28, 140]. Serological typing is technically simpler and more rapid to perform but is less suited to the testing of large numbers of strains because of the difficulty in reading the agglutination reactions. Much of the work in phage-typing can be done by junior technicians and the plates can be inspected at convenience. *Morag C. Timbury*

MAI, K. Eine neue Methode zum Nachweis bakterieller Fibrinolyse. [**A New Method for Demonstrating Bacterial Fibrinolysis**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 3/4, 291–4. [21 refs.]

For the recognition of fibrinolysin production by staphylococci or streptococci fibrinogen agar plates are prepared by adding to heparinized plasma sufficient protamine to neutralize the anticoagulant effect of the heparin, and pouring the mixture with melted agar in a Petri dish. Cultures under test are spot inoculated and, after overnight incubation, those producing fibrinolysin are surrounded by a zone of clearing.

R. E. O. Williams

DELMOTTE, A. L'activité lipolytique microbienne décelée par la méthode de Sierra avec référence spéciale au *M. pyogenes* var. *aureus.* [**Bacterial Lipolysis Determined by Sierra's Method with Special Reference to** *Staphylococcus aureus*] *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1958, v. 24, Nos. 3/4, 309–20.

In SIERRA'S method for determining lipolysis [this *Bulletin,* 1957, v. 32, 885] detergents of the Tween series are incorporated at about 1% in an agar medium together with calcium chloride (0·1 gm. per litre). Plates of this medium are surface-inoculated and incubated at 37°C. The colonies of lipolytic organisms

are surrounded by a halo, due to the precipitation of calcium soaps. Tween 20, 40, 60 and 80, and Emullat R40 and O6 were used in this way. 56 strains of *Staphylococcus aureus* were tested on this series of substrates; 28 produced visible haloes on all in 24 hours; the remainder produced various patterns of activity and 4 were quite inactive. *R. E. O. Williams*

JACKSON, A. W. & LITTLE, R. M. **Staphylococcal Toxins. II. Factors affecting Hemolysis by δ-Lysin.** *Canadian J. Microbiol.* Ottawa. 1958, Oct., v. 4, No. 5, 435–44, 4 figs. [16 refs.]

Cultures of *Staphylococcus aureus* producing α- and δ-haemolysis were grown on Cellophane sheets laid on an agar plate; the growth was extracted in saline and the δ-lysin was partially purified by precipitation with methanol. Haemolytic activity was usually determined on human red blood cells.

Preliminary experiments, in which α-antitoxin was added to the reaction mixture, showed that α-haemolysin did not interfere with δ-haemolysin. No *p*H optimum for δ-lysin could be determined; its activity was minimal at *p*H 6·8–7·3. The action of the haemolysin was initially very rapid and then suddenly ceased; this was apparently due to an inhibitory effect of the red cell ghosts and haemoglobin. Haemolysis was linearly related to lysin content over a 4-fold range of concentration. Erythrocyte concentration had a notable effect on degree of haemolysis. Serum protein, especially globulin, inhibited the haemolysin.

[For Part I of this series, see this *Bulletin*, 1957, v. 32, 805.] *R. E. O. Williams*

JACKSON, A. W. & LITTLE, R. M. **Staphylococcal Toxins. III. Partial Purification and some Properties of δ-Lysin.** *Canadian J. Microbiol.* Ottawa. 1958, Oct., v. 4, No. 5, 453–61. [16 refs.]

Attempts were made to separate the α- and δ-haemolysins of *Staphylococcus aureus*; heating to 60°C. for 5 minutes inactivated all the α-lysin but only a proportion, varying somewhat with the strain, of the δ-lysin. It is postulated that "δ-haemolysin" comprises a heat-labile and a heat-stable fraction. The δ-lysin could be concentrated by freeze-drying, but a more satisfactory method was found to be by ethanol precipitation at *p*H 4·0 and −5°C. The haemolysin could be extracted from the precipitate in buffer at *p*H 6·8, or with 75% ethanol in buffer. The final lysin is heat-stable. δ-haemolysin was held back on a sintered-glass filter but only 50% could be recovered from it. *R. E. O. Williams*

JACKSON, A. W. & MAYMAN, D. **Staphylococcal Toxins. IV. Factors affecting Hemolysis by β-Lysin.** *Canadian J. Microbiol.* Ottawa. 1958, Oct., v. 4, No. 5, 477–86, 4 figs. [12 refs.]

It was found satisfactory to test for staphylococcal β-haemolysin activity by incubating the toxin with sheep erythrocytes for 25 minutes, followed by refrigeration for 15 minutes, and, after spinning the tubes, measuring the haemolysis with a spectrophotometer. By this technique it was found that the haemolytic activity of the toxin could be largely removed by dialysis, and subsequently restored by magnesium ions; conversely the activity was reduced by citrate or by Versene. The optimum *p*H appeared to be around 7·0. The relation between haemolysis and lysis concentration was approximately linear over the range 10–75% haemolysis. Haemolytic activity was increased by the addition of serum and slightly decreased by glucose. Red cells from sheep were far more sensitive to the haemolysin than those of rabbit or man. *R. E. O. Williams*

KIENITZ, M. & PREUNER, R. Über den Nachweis des Staphylokokken-Enterotoxins. 2. Untersuchungen zur Wirkung enterotoxinbildender Staphylokokken auf Hühnerembryonen. [**The Demonstration of *Staphylococcus* Enterotoxin. 2. Study of the Effect of Enterotoxin-Producing Staphylococci on Chick Embryos**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 3/4, 203–12. [12 refs.]

Fertile hens' eggs were inoculated by the allantoic route with cultures of staphylococci. No difference in the rate at which they killed the embryos could be found between staphylococci reputed to produce enterotoxin and those that were found not to do so. The cause of death was not discovered but was evidently neither β toxin nor coagulase, and was probably not exclusively α toxin. Infected embryos could be protected with erythromycin. *R. E. O. Williams*

PRIVAT DE GARILHE, M., FASSINA, Giuliana, POCHON, F. & PILLET, J. Purification de la désoxyribonucléase de *Micrococcus pyogenes*. [**Purification of the Deoxyribonuclease of *Staphylococcus aureus***] *Bull. Soc. Chimie Biol.* 1958, v. 40, No. 12, 1905–10, 1 fig. [11 refs.]

HAYASHI, J. A. & BARKULIS, S. S. **Studies of Streptococcal Cell Walls. III. The Amino Acids of the Trypsin-Treated Cell Wall.** *J. Bacteriology.* 1959, Feb., v. 77, No. 2, 177–84, 1 fig. [31 refs.]

PAVLOV, P. V., AKIMOVA, V. V. & POMIANKEVICH, A. N. **Purified Adsorbed Scarlet Fever Toxin.—I. The Production and Purification of High Titre Scarlet Fever Toxin.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 11/12, 1637–40, 4 figs. [Translated from Russian.]

Scarlet fever toxin was produced by the Cellophane sac method devised by GLADSTONE [this *Bulletin*, 1949, v. 24, 529], titres of up to 5×10^6 skin test doses per ml. being obtained. All the toxin was contained within the sac. Toxin was purified by repeated precipitation with alcohol. With 11 such cycles, a titre of 240×10^6 skin test doses per mgm. N was obtained, although the yield was only 40%. Paper electrophoresis indicated that this preparation was substantially pure.

R. E. O. Williams

VVEDENSKAIA, O. I. **Determination of M Antibodies in Streptococcal Antisera.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 11/12, 1690–95. [20 refs.] [Translated from Russian.]

This paper describes the methods used for the preparation of antisera in rabbits to the M antigen of group A streptococci, and the tests used to verify that the precipitin reaction was in fact due to M-anti-M. The susceptibility of the M antigen to trypsin digestion was employed. *R. E. O. Williams*

WILLIAMS, A. K. & EAGON, R. G. **Oxidation of 2-Deoxy-D-Glucose to 2-Deoxy-D-Gluconic Acid by Extracts of** *Pseudomonas aeruginosa*. *J. Bacteriology*. 1959, Feb., v. 77, No. 2, 167–72, 3 figs. [14 refs.]

MCCULLOUGH, N. B. & BEAL, G. A. **The Biological Stability of the Genus** *Brucella*. *Bull. World Health Organization*. Geneva. 1958, v. 19, No. 4, 725–37. [31 refs.]

The authors maintain that the 3 classical species (*melitensis, abortus* and *suis*) of the *Brucella* genus are definitely distinguishable on the basis of their origin, CO_2 requirements, resistance to dyes and production of H_2S. Serological typing procedures have considerable limitations and may be confusing, especially through lack of homogeneity in *melitensis* strains and through dissociation of cultures used in the preparation of monospecific sera. CO_2 requirement by *Br. abortus* on primary isolation is the most distinctive species characteristic; dye resistance is the most reproducible test and determination of urease activity is only a supplementary test. Tests being only quantitative, techniques have to be rigidly standardized and controlled and, even so, no one test is dependable for species identification. The authors believe no organism should be considered for inclusion in the *Brucella* genus which is not morphologically similar and closely related antigenically to existing members.

In recent years, after scattered reports of change of species after experimental infection of animals and of isolation of atypical strains, members of the *Brucella* genus have been said to be labile in their species characteristics. Cases of *in vivo* species mutations represent, according to the authors, "undetected infections in the experimental animals prior to use, cross-infection, or technical errors." The authors quote their own experiments and those of others which demonstrate impressively the *in vivo* immutability of species. Had it been otherwise, there would have been many distinguishable species. Reviewing their work over the past 17 years, the authors state that many "aberrant" *Brucella* strains represent in fact only aberrations in applying the typing procedures. Complete stability of characteristics *in vitro* was seen in 34 cultures maintained over 9 years. *E. Agius*

RENOUX, G. Considérations sur la notion d'espèce dans le genre *Brucella*. [**Some Considerations on the Concept of Species in the** *Brucella* **genus**] *Bull. World Health Organization*. Geneva. 1958, v. 19, No. 4, 739–45.

According to one view there are only 3 species of *Brucella*, no variations have been demonstrated and serological identification is of no value; according to the other, considering the close resemblances which exist between the various strains, there is only one species, *Brucella melitensis*. In an other article [*Ann. Inst. Pasteur*, 1958, v. 94, 179] the author had concluded that there are no criteria by which one can easily differentiate the various *Brucella* species. Separation of *Brucella* into distinct species on the accepted lines would provide the only example of a classification solely dependent on quantitative criteria. Classification on the basis of dependence on CO_2 for primary isolation, resistance to dyes, production of H_2S, and reaction with monospecific sera gives at least 4 species, including *Br. suis* (with its Danish variety) and *Br. intermedia*, but the data from the use of these criteria could be arranged in 64 combinations. Only 3 or 4 arrangements have been accepted as of value in classification on the basis of statistical frequency.

The real problem lies in determining which criteria should be given specific value. If the characters usually accepted have real value there should be as many species as there are possible combinations. It is difficult to attribute any value either to the geographical origin or to the animal from which the strain derives, nor does epidemiology afford any more valid criterion. No bacteriological classification can depend on merely practical considerations or on characteristics subject to mutations. The object of any classification cannot be attained if the choice of criteria determining a species is arbitrary. In the present state of our knowledge it seems wisest to consider that there is only one species, *Br. melitensis* Bruce. Study of varieties will be of use epidemiologically; the important point is to realize the basic clinical and bacteriological unity of brucellosis. *E. Agius*

ELBERG, S. S. & MEYER, K. F. **Caprine Immunization against Brucellosis. A Summary of Experiments on the Isolation, Properties and Behaviour of a Vaccine Strain.** *Bull. World Health Organization*. Geneva. 1958, v. 19, No. 4, 711–24, 4 figs. 7 tables. [12 refs.]

A strain of non-streptomycin-dependent *Brucella melitensis* mutating from an originally dependent strain was found to be capable in the living state of immunizing mice and guineapigs, possessing the necessary powers of growth and persistence. Freeze-drying in a final concentration of 3% lactose resulted in a 25% loss of the original bacterial population, but the preparation was stable for at least 2–3 months. Goats injected subcutaneously with $1{\cdot}5 \times 10^9$ cells of the vaccine strain were found gradually to have cleared their tissues by the 14th week and no bacteria could be detected in the blood, in 18 animals, later than the 7th day. Antibodies appeared within 10 days, but, throughout these experiments the agglutination titre was found to provide little information as to the animal's infection status, though abortion was often preceded by a dramatic rise.

The immunizing power of the vaccine was tested by subcutaneous administration of $1{\cdot}5 \times 10^9$ viable cells to 13 goats, and the same number of heat-killed cells to 12 others. 12 weeks later both sets were given a booster dose of 2×10^9 heat-killed cells. The

challenge dose was 33 times the ID50 (830,000 cells), given 3 to 4 weeks later. Mating was carried out 2 months after the first injection and completed about 2 weeks before the challenge dose was given. No infections, no abortions, and no infected kids resulted in the goats given the live vaccine. 10 out of 12 of those given the killed vaccine showed infection and 9 abortions and 1 infected kid resulted. In 12 controls there were 10 infections, 9 abortions and 1 infected kid. The vaccine appeared effectively to prevent abortion when given as late as 2 days after mating, but 2 abortions in 5 goats resulted when it was given 35 days after mating.

At the cellular level, it was observed that when virulent brucellae in normal serum are ingested by mononuclear cells of normal or vaccinated rabbits, the monocytes are destroyed, whereas when monocytes from vaccinated rabbits ingest brucellae suspended in Tyrode solution containing serum from vaccinated rabbits they are not destroyed; on the other hand, serum from vaccinated rabbits cannot protect monocytes from unvaccinated animals. A variety of antisera are capable of enhancing aspecifically the resistance of monocytes from vaccinated animals. It appears that resistance to brucellae is non-specific in the sense that it covers more than one organism, but specific in as much as it applies to parasites which are intracytoplasmic during the infection. *E. Agius*

REUSSE, U. Über die Dissoziation von Brucellen. [**Dissociation of Brucella**] Parts I & II. Reprinted from *Monats. f. Tierheilk.* 1958, v. 10, Nos. 10 & 11, 135–40; 143–50. [73 refs.]

VAKE, A. **The Variation of Plague Bacilli (Strain *Pasteurella pestis* EB) in the White Mouse.** *J. Microbiol., Epidemiol & Immunobiol.* London. 1957, v. 28, Nos. 11/12, 1803–6, 2 figs. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1959, v. 56, 609.]

CLARKE, Patricia H. & MEADOW, Pauline M. **Evidence for the Occurrence of Permeases for Tricarboxylic Acid Cycle Intermediates in *Pseudomonas aeruginosa*.** *J. General Microbiol.* 1959, Feb., v. 20, No. 1, 144–55, 4 figs. [21 refs.]

TAUBER, H. & GARSON, W. **Effect of Sonic Energy, Ultracentrifugation, and Phenol on *Neisseria gonorrhoeae* Endotoxin.** *Proc. Soc. Exper. Biol. & Med.* 1958, Dec., v. 99, No. 3, 675–7, 1 fig.

This is a highly technical article which will be of interest mainly to biochemists.

Gonococci were cultured and submitted to sonic treatment and ultracentrifugation. 7 different fractions were obtained and found to have LD50 values for mice varying from 0·8 to 2·3 mgm.

A protein-free endotoxin was prepared by treatment with phenol-water mixture and precipitation with acetone; this had an LD50 of 0·8 mgm. and contained 52% saccharide, 53% nucleic acid and 8·5% nitrogen.

Sonic disintegration puts 90% endotoxin into a soluble state and the various fractions do not differ much in toxicity but are more toxic than the product obtained by alkaline extraction; phenol-water removes the protein from the nucleoprotein complex of gonococcus endotoxin; the protein-free endotoxin contains mainly polysaccharide and nucleic acid; the dried product is more toxic than those obtained by other methods.

For details of the various extractions the original should be consulted. *T. E. Osmond*

BOREL, L. J., BENTEJAC, R. & DUREL, P., with the technical assistance of J. MARIEN. **Lyophilized Survival Medium for the *T. pallidum* Immobilization Test.** *Brit. J. Venereal Dis.* 1958, Dec., v. 34, No. 4, 241–5, 2 figs.

The keeping qualities of survival medium are very important factors in carrying out TPI tests. These authors used a standard medium (details are given in a table) which contained dihydrostreptomycin, human, rather than bovine, albumin and penicillinase and increased amounts of ultra-filtrate of ox serum. The details of preparation are given in the text

After filtration the medium is immediately frozen in 10 ml. amounts in 30 ml. ampoules which are sealed *in vacuo*; for use the ampoule is opened and the required amount of double distilled water is added.

This medium kept well at room temperature indefinitely and was found to be as good as non-lyophilized medium kept at −20°C.; it is essential that the medium be kept in completely air tight containers.

Repeated trials in the authors' own and in other laboratories showed that lyophilized medium was quite satisfactory. If poor results in the TPI test are obtained it seems almost certain that the nature of the orchitis in the syphilitic rabbits is the cause.

It is concluded the lyophilized medium has many advantages particularly in laboratories where its manufacture is difficult or impossible. *T. E. Osmond*

FISCHER, G. W., POWERS, Dorothy K. & GALTON, Mildred M. **Studies of Technics for the Isolation of Leptospires. I. The Suitability of 1 to 2 Day Old Baby Chicks as compared to Hamsters for the Isolation of Various Leptospiral Serotypes.** *J. Infect. Dis.* 1958, Sept.–Oct., v. 103, No. 2, 150–56, 4 figs.

To determine the relative susceptibility of baby chicks and weanling hamsters (18–25 days old) to infection with leptospires, groups of 3 chicks and 3 hamsters were inoculated intraperitoneally with cultures of old stock strains of the following serotypes: *Leptospira andaman, L. autumnalis, L. ballum, L. bataviae, L. canicola, L. grippotyphosa, L. hebdomadis, L. hyos, L. icterohaemorrhagiae, L. pomona, L. pyrogenes, L. sejroe, L. sentot* and *L. wolffii.*

Blood for culture was obtained by cardiac puncture on 5 occasions at intervals of a few days up to the end of the 3rd or 4th week. Positive blood cultures were obtained from both hamsters and chicks with 10 serotypes. *L. andaman* did not infect either [according to the table, though the text states it was recovered from

hamsters]. Positive cultures of *L. grippotyphosa* were obtained only from hamsters, and *L. ballum* and *L. icterohaemorrhagiae* only from chicks. Recently-isolated strains of the last 2 serotypes did, however, cause leptospiraemia with positive cultures, but similar strains of the other 2 were not available.

In a field investigation samples of urine from suspected cases of leptospirosis in human beings, dogs and cattle were inoculated into either hamsters or chicks. A certain number of strains were isolated but the same specimens of urine were not inoculated into both hamsters and chicks so the relative values of the 2 species could not be determined. [Methods of increasing the susceptibility of chicks to infection are described by HOWARTH and REINA-GUERRA, below.]

J. C. Broom

PIKE, R. M. & SCHULZE, Mary L. **Serologic Variants of Leptospira Types resulting from Growth in Immune Serum.** *J. Immunology.* 1958, Aug., v. 81, No. 2, 172–5. [10 refs.]

Attempts were made to induce serological variation by growing strains of *Leptospira grippotyphosa, L. canicola* and *L. pomona* in culture medium containing rabbit homologous antiserum. Antiserum dilutions of 1/100–1/1,000 were used for the early transfers, and the concentration was then gradually increased to 1/20 or 1/10. In the first few subcultures most of the leptospires were agglutinated into large clumps but a few free individuals were always present also. These were used for seeding the next subculture because it has long been known that the progeny of such inagglutinable leptospires are in no way abnormal [SCHÜFFNER and MOCHTAR, *Tropical Diseases Bulletin*, 1927, v. 24, 714].

The strain of *L. grippotyphosa* was carried through 39 subcultures over a period of 3 years: the initial subculture was made in 1/1,000 antiserum and the last in 1/10. The agglutinin titre of the antiserum against the untreated strain was 40,960: after 11 subcultures the antiserum agglutinated the treated strain only in dilutions up to 1/800, and after 20 passages to 1/40 at which level the titre remained up to the 39th subculture.

Cultures made from the 20th passage in normal medium were used to prepare an antiserum for comparison with the original strain. Its titres with the treated and original strains were 40,960 and 1,280 respectively. In cross-absorption tests each strain only slightly reduced the titre of the heterologous serum for its homologous antigen.

Similar results were obtained with *L. pomona* and *L. canicola* when rabbit antisera were used: serum (titre 6,400) from a guineapig which had survived infection with *L. canicola* had no effect after 17 transfers over 9 months in a 1/100 dilution.

After the last transfer in immune serum, the strains were subcultured in normal medium for 8 months. When retested then, the agglutination reactions had not altered, showing that the treated strains had no tendency to revert to their original serological behaviour.

Since these serological changes occurred only after prolonged culture in the presence of immune serum, it seems likely that they are due to selection of mutants which occur extremely rarely. Animal carriers of leptospires usually have detectable antibodies in the blood and tissue fluids: the authors suggest that if mutations occur *in vivo* some mutants might have an advantage over the original antigenic type and so give rise to new antigenic types. [An alternative hypothesis to explain the emergence of new serotypes was put forward by GSELL (*Revue Médicale de la Suisse Romande*, 1949, v. 69, 613). He suggested that adaptation to a new carrier host, whose protein metabolism differed to some extent from that of the normal host, might induce metabolic changes in the leptospires which could alter their antigenic compositions.]

J. C. Broom

HOWARTH, J. A. & REINA-GUERRA, M. **Comparative Studies on Experimental Avian Leptospirosis.** *J. Infect. Dis.* 1958, May–June, v. 102, No. 3, 268–74. [11 refs.]

HOAG *et al.* [this *Bulletin*, 1954, v. 29, 107] showed that 2-day-old chicks could be infected with *Leptospira pomona* by intraperitoneal inoculation of infective material, and they suggested that chicks might prove useful for isolating strains of leptospires. The present authors extended these studies to include also *L. canicola* and *L. icterohaemorrhagiae*, and also sought for methods of increasing the susceptibility of chicks to infection.

When strains of the 3 serotypes, which were highly virulent for hamsters, were injected parenterally into chicks, a leptospiraemia regularly developed about a week after the inoculation, but the birds showed no signs of illness. There was no transmission of infection to normal chicks housed along with the infected ones.

The degree of leptospiraemia was estimated by direct counts on cell-free plasma. The findings indicated that the numbers of the 3 serotypes present per ml. were roughly *L. pomona* $0{\cdot}33 \times 10^5$, *L. canicola* $0{\cdot}93 \times 10^5$ and *L. icterohaemorrhagiae* $1{\cdot}92 \times 10^5$.

The number of leptospires circulating in the blood was considerably increased when chicks were deprived of food, but not water, for the first 3½ days of life, and also when they were exposed to non-lethal doses of X-ray radiation. The birds, however, did not die of leptospirosis. [PETROV, *ibid.*, 1958, v. 33, 796, found that fatal infections could be produced in irradiated rabbits, mice and guineapigs by strains of leptospires which were non-virulent in normal control animals.]

J. C. Broom

BAUER, D. C. & MORSE, E. V. **Variation and Hemolysin Production in relation to Virulence of** *Leptospira pomona. Proc. Soc. Exper. Biol. & Med.* 1958, July, v. 98, No. 3, 505–8, 1 fig. [18 refs.]

In the experiments reported here, 2 strains of *Leptospira pomona* were used: strain W, which had been maintained by serial passage in weanling guineapigs, was not lethal for hamsters; and strain O, which had been maintained in guineapigs and hamsters, was lethal for both species. Blood-cultures of each strain

were made from infected animals, and were subcultured when growth was optimal. The numbers of leptospires present in the cultures were estimated by direct counting, and 10-fold serial dilutions were prepared. Groups of 5 young hamsters were inoculated intraperitoneally with 1·0 ml. amounts of each dilution, except for the first subculture of strain W when 7 animals were used.

The hamsters were kept under observation and, if they became infected, blood was obtained by cardiac puncture when they were moribund and examined microscopically for the presence of leptospires. Animals which survived were killed after 20–30 days and their sera tested for agglutinins. The virulence of each culture was expressed as the number of leptospires which would kill 50% of inoculated hamsters (LD50).

The virulence of strain W was tested for subcultures 1, 4, 8, 10, 12, 16, 20 and 24. None of the hamsters died after inoculation with any dilution of subculture 1, but deaths occurred in all subsequent titrations (*i.e.* subcultures 4–24), though there were irregular variations in the virulence of successive subcultures. Virulence determinations on subcultures 1, 4, 7 and 11 of strain O indicated an initial decrease followed by an increase.

The authors suggest that these fluctuations in virulence (as estimated by LD50 doses) might be explained by postulating that conditions in some subcultures favour a faster growth rate of less virulent mutants, and that in other subcultures the reverse is the case. [In this type of experiment there are, however, so many uncontrollable factors which might influence the results that it seems inadvisable to lay too much emphasis on any single one.]

The second series of experiments was designed to show whether there was any correlation between virulence and the ability to produce the haemolysin which was demonstrated in cultures of certain strains of leptospires by ALEXANDER *et al.* and by RUSSELL [this *Bulletin*, 1956, v. 31, 953; 1957, v. 32, 998]. Tests made with 3 virulent and 2 nonvirulent cultures of strain W and 2 virulent cultures of strain O showed no evidence of correlation between these 2 characters.

J. C. Broom

GERHARDT, Mary R. & BALL, M. G. **Amino Acid Utilization by** *Leptospira canicola*. *J. Bacteriology*. 1959, Jan., v. 77, No. 1, 17–22, 2 figs. [13 refs.]

STOENNER, H. G., GRIMES, E. F., THRAILKILL, F. B. & DAVIS, E. **Elimination of** *Leptospira ballum* **from a Colony of Swiss Albino Mice by use of Chlortetracycline Hydrochloride.** *Amer. J. Trop. Med. & Hyg.* 1958, July, v. 7, No. 4, 423–6.

It had long been known that *Leptospira ballum* was present in the breeding colony of mice at the Rocky Mountain Laboratory, but no steps were taken to eradicate the infection until it was realized that a number of workers in the laboratories had contracted leptospirosis [STOENNER & MACLEAN, this *Bulletin*, 1958, v. 33, 749]. The size of the breeding stock (some 10,000 strong) precluded the possibility of building up a clean colony by segregating the young of *infected* dams at 21 days of age [the original should be consulted by those interested for the details of this most ingenious method]. An attempt was made therefore to eradicate the infection by treating the whole stock with chlortetracycline which was considered the antibiotic most likely to be effective.

Preliminary experiments showed that a dose of 5 mgm. daily for 7 days would eliminate leptospires from the kidneys of infected mice, and that the drug increased rather than diminished fertility. For treatment of the stock, pelleted feed was prepared containing 1,000 gm. of chlortetracycline hydrochloride per ton and was fed to the mice for 10 days.

Periodically, after treatment, groups of discarded breeding females were examined, and *L. ballum* was not recovered from any of these mice. Though this is not conclusive proof it is regarded as strong presumptive evidence that the treatment had eliminated the infection.

J. C. Broom

VOROB'EV, A. A. **Therapeutic Action of Various Preparations of Tetanus Toxoid in relation to the Method of Injection.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, Nos. 3/4, 432–7, 1 fig. [13 refs.] [Translated from Russian.]

The possibility of protecting mice from tetanus toxin by simultaneous or immediately subsequent injection of tetanus toxoid already described by other workers is confirmed. The dose for protection of a mouse from 1 MLD of toxin is 20 Lf toxoid but only if it is given by the intravenous route. More is required by the intraperitoneal route.

The most interesting point brought out in this study is that if groups of mice are injected intravenously on the same day with 50 Lf of purified and concentrated toxoid, the mortality, which is nil if toxin injection follows that of the toxoid within 5 hours, is almost equal to that of the controls when the interval between toxoid and toxin injection is 3 days; but with a longer interval before administration of toxin it steadily falls till after a 14-day interval more than 90% of mice survive the injection of toxin although some of them show signs of tetanus.

There are thus 2 periods in the toxoid protection—an early and a late one—but no explanation is offered. The early protection does not, however, leave the mice apparently symptomless and normal in the same way that an adequate dose of antiserum does.

J. W. McLeod

MARTINEZ, R. J. & RITTENBERG, S. C. **Glucose Dissimilation by** *Clostridium tetani*. *J. Bacteriology*. 1959, Feb., v. 77, No. 2, 156–63, 8 figs. [20 refs.]

WAGENAAR, R. O., DACK, G. M. & MURRELL, C. B. **Studies on Purified Type A** *Clostridium botulinum* **Toxin subjected to Ultracentrifugation and Irradiation.** *Food Research*. Champaign, Ill. 1959, Jan.–Feb., v. 24, No. 1, 57–61.

"In each of three experiments approximately 15 mg. of purified type A *Clostridium botulinum* toxin in 5 ml. of 0.05M sodium acetate-acetic acid buffer was placed in a Visking casing and dialyzed against 0.05M sodium phosphate buffer solution at pH 7.5. The dissociated toxin was spun in an ultracentrifuge at

100,000 times gravity for 3 hours at 0°C. to separate it into two components.

"Appropriate dilutions of the whole toxin and of each of the components were irradiated in sealed glass vials at several dosage levels with Cobalt-60 to establish their inactivation patterns. The radiation levels required to inactivate the whole purified toxin and the two components separated by ultracentrifugation were established by intraperitoneal injection of appropriate dilutions of the toxin into 16 to 20 gram white mice.

"There was little difference in the inactivation patterns of whole purified toxin and of the two fractions. In comparable samples with an initial toxicity of 100,000 MLD per ml., about 80% of the toxicity was removed by only 3,000 rads, whereas it required 900,000 rads to inactivate 99.99% of the toxin.

"The purified toxin was approximately 100 times less resistant to radiation with Cobalt-60 than unpurified type A *Cl. botulinum* toxin in sterile trypticase broth or heat-treated surface ripened cheese. The smaller radiation dosage needed for inactivation of purified toxin may be a measure of the protection offered by the other constituents in crude toxin."

BOROFF, D. A. & REILLY, J. R. **Studies on the Toxin of *Clostridium botulinum*. V. Prophylactic Immunization of Pheasants and Ducks against Avian Botulism.** *J. Bacteriology*. 1959, Feb., v. 77, No. 2, 142–6.

MALLIN, M. L. & KAPLAN, N. O. **Uptake of P^{32} in Resting Cells of *Clostridium perfringens*.** *J. Bacteriology*. 1959, Feb., v. 77, No. 2, 125–30, 2 figs.

BEERENS, H., GUILLAUME, J. & PETIT, H. Étude de la fermentation propionique de la L(−)thréonine par 45 souches de bactéries anaérobies non sporulées à Gram négatif. **[Studies on the Proprionic Fermentation of L (−)threonin by 45 Strains of Anaerobic Non-Sporing Gram-Negative Bacteria]** *Ann. Inst. Pasteur*. 1959, Feb., v. 96, No. 2, 211–16.

"In a previous paper, the authors already suggested that the fermentative type of volatile acidity was a species-specific property of Gram-negative bacteria. In the present report they describe another species-specific character: the degradation of threonin into propionic acid. This property is not only species-specific, it also allows to distinguish four groups among bacteria of the *Spherophorus, Fusiformis* and *Ristella convexa* genera. The first one comprises the *Spherophorus*; the second one the *Fusiformis* (*fusiformis, nucleatus, polymorphus, hemolyticus*); the third one is represented by certain strains of *F. biacutus* (type II) related to those of the precedent group; the fourth one comprises the *Ristella* and the other *F. biacutus* (type I.)

"This new property confirms the homogeneity of *Ristella convexa, Spherophorus* and *Fusiformis*. It shows that *Fusiformis biacutus* must be excluded from the *Fusiformis* genus and that this species must be divided into two distinct ones. In a further paper, the authors will study the taxonomy of these two species and the properties which allow to identify them in the laboratory routine, the reaction described in the present work being difficult to perform and requiring a complex material."

BENNETT, E. O., PETERSON, G. E. & WILLIAMS, R. P. **Penicillin Sensitivity as compared with Nucleic Acid Phosphorus Content of Virulent and Avirulent Strains of *Bacillus anthracis* and *Bacillus cereus*.** *Antibiotics & Chemotherapy*. New York. 1959, Feb., v. 9, No. 2, 115–20. [16 refs.]

"The penicillin sensitivities of virulent and avirulent *Bacillus anthracis* cultures were determined by the tube dilution method. The results showed that virulent strains were uniformly sensitive. It was found that virulent strains had in general a greater deoxyribonucleic acid content, lower ribonucleic acid/deoxyribonucleic acid ratios, and greater penicillin sensitivity than did avirulent ones.

Examination of several strains of *Bacillus cereus* showed that this organism resembles avirulent *B. anthracis* strains in its resistance to penicillin and nucleic acid content."

URBÁ, Ruth C. **Protein Breakdown in *Bacillus cereus*.** *Biochem. J.* 1959, Mar., v. 71, No. 3, 513–18, 4 figs. [22 refs.]

EPSTEIN, S. S., with the technical assistance of N. SPURLING. **The Biochemistry and Antibiotic Sensitivity of the Klebsiellae.** *J. Clin. Path.* 1959, Jan., v. 12, No. 1, 52–8, 1 fig. [45 refs.]

This is a well documented account of the biochemical reactions of 82 strains of *Klebsiella*, 32 of which were from the National Collection of Type Cultures and included representatives of the species *K. pneumoniae, K. rhinoscleromatis, K. ozaenae* and *K. aerogenes*. Different techniques in carrying out the biochemical tests may give different reactions, and the author gives details or references to all the methods used in this survey. The original paper should be consulted for full details of the results but a summary is shown in the accompanying table, in which the percentage of positives is recorded for tests which showed the biggest differences between strains of the different species.

Epstein discusses the taxonomic implications of the results, and supports the suggestions of CLARKE [this *Bulletin*, 1955, v. 30, 709] and SNEATH [*ibid.*, 1957, v. 32, 1181] that the results of biochemical tests should be expressed statistically rather than on a + or − basis. *K. pneumoniae* strains are typically aerogenic and positive in lactose, citrate, VP, malonate, KCN, gluconate, and lysine tests. Type 3 usually has the reverse properties and apart from an aerogenic variant, all type 3 strains differed from all others in being sensitive to erythromycin, oleandomycin and novobiocin. In spite of these differences Epstein surprisingly does not think that they justify recognition of a separate species. As he does not regard types 4–6 as homogeneous, he will not accept *K. ozaenae*. For the single species he recognizes, Epstein recommends the name *friedländeri*. [The Bacteriological Code does not recognize appropriateness as a basis for changing a name, and the

epithet *pneumoniae* has many years' priority over *friedländeri*.] *S. T. Cowan*

Summary of differences between Klebsiella subgroups

	K. pneumoniae Serotypes 1.	*K. pneumoniae* Serotypes 2.	*K. rhinoscleromatis* serotype 3	*K. ozaenae* serotypes 4–6	*K. pneumoniae* Serotypes 8–13	Untypable	*K. aerogenes*
No. of strains	23	5	7	9	6	25	7
Mucoid colonies	91	80	85	77	100	56	0
Glucose (gas)	91	100	14	33	83	96	85
M.R.	13	40	100	100	50	4	42
V.P.	87	60	0	0	50	96	57
Urease	87	100	14	44	100	52	85
Koser's citrate	65	100	14	44	100	100	85
Indole	0	0	0	0	0	8	71
KCN	100	100	42	77	100	88	100
Gluconate	100	100	14	33	100	100	100
Malonate	47	100	71	11	66	100	85
Lysine decarboxylase	100	100	14	33	100	24	100
Sensitive to EON	0	0	85	0	0	0	0

EON = Erythromycin, oleandomycin and novobiocin

Results expressed as percentage of strains in each subgroup giving a positive result.

OSTERRIETH, P. Propriétés biochimiques des *Klebsiella*. [**Biochemical Properties of the** *Klebsiella*] *Ann. Soc. Belge de Méd. Trop.* 1958, Aug. 31, v. 38, No. 4, 721–30. [17 refs.]

This paper reports an investigation of a highly selected group of organisms having the general characters of *Klebsiella*. All motile strains or those with atypical reactions were excluded. Most of the sugars tested were fermented, only the alcohols, sorbitol, adonitol and dulcitol giving different results with different strains. Apart from the fermentations of tartaric and citric acids, which were irregular, the other reactions were either positive or negative for most of the strains. Thus all strains tested were MR −, VP +, H_2S −, lysin decarboxylase +, KCN +, ammonia and citrate utilization +. Most strains were gelatin −, urea + and indole −.

There were no significant differences between strains isolated from man or chimpanzees. The biochemical tests were used to classify the 142 strains; 118 fell within the 36 biotypes defined by ØRSKOV [this *Bulletin*, 1957, v. 32, 990] and 13 new biotypes were created for the other strains. *S. T. Cowan*

HARTWIGK, H. Die S-Form der *Listeria monocytogenes* im Vergleich zu Kolonien listeriaähnlicher Keime. [**The Colonies of** *Listeria monocytogenes* **in S-Form Compared with those of Various Bacteria Resembling** *Listeria*] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 7/8, 568–80, 7 coloured figs. on pl.

This work is a follow-up of GRAY'S observations [this *Bulletin*, 1958, v. 33, 522] that under oblique illumination of a surface culture on tryptose agar the colonies of *Listeria monocytogenes* are characteristic in colour, texture and outline.

The strains used in this investigation included Patterson's 4 types of *Listeria*, 3 strains of type 4B, 5 type I (3 from man, 1 from the ox and 1 from the hen). These were compared with the following strains taken from a stock collection— *Erysipelothrix muriseptica* and the following species of *Corynebacterium*— *pyogenes bovis, renale* and *diphtheriae* (*mitis* and *gravis*); also with *Diplococcus lanceolatus, Streptococcus pyogenes* (group C), *Brucella abortus* and *Pseudomonas pyocyanea* and were used after repeated subcultures.

The appearances of all these on the tryptose agar are described in considerable detail and also the appearances of most of them in the same medium reinforced with various percentages of potassium tellurite. There are also descriptions of the appearances of the colonies on horse meat extract agar reinforced with horse serum and also on Kröger's saccharose indicator plate.

The net outcome of these investigations is to show that colonies of *E. muriseptica* and *C. pyogenes* may show a considerable resemblance in colour to those of *Listeria* and that the former may also resemble *Listeria* colonies in texture. It is claimed, however, that Kröger's medium gives a sharper differentiation of *Listeria* from *E. muriseptica* and the various corynebacteria.

There is an interesting colour plate illustrating a number of the appearances which are described.

J. W. McLeod

FUNGI

DONALD, G. F. **Tinea Capitis in South Australia: a Preliminary Statment of Cultural Findings.** *Med. J. Australia.* 1958, Oct., 4, v. 2, No. 14, 452–4. [14 refs.]

In Australia most cases of tinea capitis are due to the zoophilic fungus *Microsporum canis*, a parasite of dogs and cats, which is responsible for more than 70% of the infections seen in man. Many of these cases clear within 6 months but persistence for more than 12 months is well known. *M. audouini* produces a similar clinical condition but spontaneous cure is rare before puberty.

The remaining fungi are members of the genus *Trichophyton*, of which the group producing endothrix spores is the more important, the commonest member being *T. tonsurans*.

Culture of 81 cases of tinea capitis at the Royal Prince Alfred Hospital, Sydney in 1952–1953 showed that 65 were due to *M. canis*, 15 to *T. tonsurans* and 1 to *T. violaceum*; of 142 cases of tinea capitis cultured at the Adelaide Children's Hospital between 1954 and 1957, 125 were due to *M. canis*, 15 to *T. tonsurans* and 2 to *T. violaceum*.

M. audouini infections are common in cold climates but no case was detected among cultures from 200 consecutive cases of tinea capitis in Australia.

H. T. H. Wilson

DUNCAN, J. T. **Tropical African Histoplasmosis.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1958, Sept., v. 52, No. 5, 468–74, 9 figs. on 2 pls. [22 refs.]

This paper gives a brief description of the clinical features of the first case of African histoplasmosis (in a 63-year-old mining engineer in Ghana), which was diagnosed by Duncan in 1943 but never fully described [see this *Bulletin*, 1953, v. 28, 628–9], and a detailed study of the pathogen which VANBREUSEGHEM in 1952 [*loc. cit.*] independently described as *Histoplasma duboisii*.

It is concluded that African histoplasmosis is a histopathological entity and that while the species *H. duboisii* rests on a very slender basis its identity should be preserved either as a species or, as suggested by others, as a variety of *H. capsulatum*.

G. C. Ainsworth

WANG, C. J. K., SCHWARZ, J. & BAUM, G. L. **Large Forms of *Histoplasma*.** *Mycopathologia.* The Hague. 1958, Dec. 30, v. 10, No. 2, 53–70, 12 figs. [32 refs.] [Summary taken from *Rev. Med. & Vet. Mycol.*, 1959, June, v. 3, Pt. 6, 189.]

At the Jewish and General Hospitals, Cincinnati, the development of the laminated, onion-like, large forms of *H. capsulatum* [this *Bulletin*, 1956, v. 31, 587 *bis*] was studied in hamsters injected intraperitoneally with the yeast phase. To compare *H. capsulatum* with *H. duboisii*, 6 groups of animals (10 hamsters and 10 mice/group) were injected intraperitoneally with 6 strains. The growth of large forms in tissue explants was studied, hamsters being infected intraperitoneally with the yeast phase of both organisms.

The evidence obtained demonstrated that in the yeast phase there are 5 distinct forms of *Histoplasma*: the classical *H. capsulatum* form, ovoid and 2–5 μ; occasional "large" forms, mostly measuring 6–9 μ, found in necrotic tissue and old cultures; induced giant forms in tissue explants, up to 20 μ; small or large yeast cells surrounded by a halo, up to 30 μ; and, finally, the *duboisii* form, up to 22 μ or more, found in *H. duboisii* only. The large forms of *H. capsulatum* obtained in tissue explants resemble the form found in necrotic human tissue; they have thinner cell walls than the large cells of *H. duboisii*. Most strains of *H. capsulatum* are pathogenic to mice and hamsters. *H. duboisii* does not cause death in mice, but produces progressive organ involvement in mice and hamsters and occasionally death in hamsters.

H. duboisii and the "classical" *H. capsulatum* can be separated by size in the parasitic phase *in vivo* and *in vitro*; by their differences in pathogenicity for experimental animals; and by the most particular tissue response in hamsters and mice.

SCHMIDT, E. G. & THORP, Patricia. **The Effect of Chemotherapeutic Agents upon the Growth of *Cryptococcus neoformans*.** *J. Infect. Dis.* 1958, Sept.–Oct., v. 103, No. 2, 142–4.

Experiments showed that the action of 8-hydroxyquinoline (oxine) on *Cryptococcus neoformans in vitro* was not antagonized by ions of cobalt, copper, zinc, manganese or iron.

Of 202 organic compounds (which are listed) tested *in vitro* for inhibitory activity against *C. neoformans*, rimocidin, 1-(2-phenyl-2-hydroxyethyl)-4-(1-octyl)-piperidine (both inhibitory at 0·001 mgm./ml. of agar) and several other less active compounds are considered to merit further study against infections of experimental animals.

G. C. Ainsworth

RICKETTSIAE

ZDRODOVSKII, P. F., GOLINEVICH, E. M. & IABLONSKAIA, V. A. **The Characteristics of Strain E of *Rickettsia prowazeki* and its Pathogenic Properties.** *Problems of Virology.* London. 1958, v. 3, No. 3, 145–51. [Translated from Russian].

ZDRODOVSKII, P. F. **The Problem of Live Typhus Vaccine.** *Problems of Virology.* London. 1958, v. 3, No. 3, 141–5. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 602.]

BREZINA, R. **A Change in the Virulence of the Henzerling Strain of *Coxiella burneti* during Passage in White Mice.** *Acta Virologica.* Prague. 1958, Oct.-Dec., v. 2, No. 4, 220–27. [12 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 604.]

BACTERIOPHAGES

FILDES, P. & KAY, D. **The Function of Tryptophan in the Adsorption of a Bacteriophage.** *Brit. J. Exper. Path.* 1959, Feb., v. 40, No. 1, 71–9, 6 figs. (2 on 2 pls.) [10 refs.]

A mutant (tryp+) of phage 3 which required tryptophan for adsorption to bacteria [this *Bulletin*, 1958, v. 33, 524] and to isolated bacterial receptors, was also found to require tryptophan for its adsorption to various mineral particles. Electron micrographs showed that the phage particles adsorbed by their tail tips to the minerals. Inactivation of tryp+ by heat, by antiserum and by papain, was greater in the presence of tryptophan. The presence of tryptophan made no difference to the effect of these agents on tryp−, a mutant which did not require tryptophan for adsorption to bacteria.

When papain was activated by cysteine and its protease activity was therefore greatest, much less phage was inactivated than when the enzyme's proteolytic action was least. It seems likely that it was the thiolesterase activity of papain which was concerned with phage inactivation.

The authors suggest that thiolester bonds known to exist in the phage tail tip are the target for other inactivating agents as well as papain. They suggest that tryptophan causes the exposure of thiolester bonds maintaining the structure of the tryp+ phage tail and this is followed by their rupture and phage inactivation. The tryp− mutant may have tryptophan bound to the reacting sites on the tail tip, so that thiolester bonds would be permanently exposed and the presence of excess tryptophan would not influence the reactions of the tail tip. *Janice Taverne*

SALLES, C. A. **Adsorption of Bacteriophage T1 on Heat Inactivated** *E. coli*. *Anais Acad. Brasileira de Ciências*. 1958, Sept. 30, v. 30, No. 3, 327–35, 3 figs. [23 refs.]

The rate of adsorption of T1 phage to *Escherichia coli* B cells which had been heated to different temperatures was compared with the rate of adsorption to normal cells. Adsorption was irreversible and did not occur with cultures which had been heated to 55°C. or over, *i.e.* in which all the cells were killed. Adsorption of T1 was shown to depend upon the viability of the cells.

The coefficient of adsorption of T1Hr, a host range mutant was constant even with cells heated as high as 90°C. The adsorption of T1Hr to normal and heat killed cells was irreversible. It is suggested that the irreversible adsorption of T1 to *E. coli* B involves an enzymatic reaction and that the same adsorption of T1Hr, which is controlled by the Hr gene, does not. *Janice Taverne*

FRANCQ, J. C., EYQUEM, A. & GUYOT-JEANNIN, N. Le pouvoir inhibiteur de sérum vis-à-vis du bactériophage T2 r + et la properdine. [**Inhibitory Capacity of Serum towards T2r + Phage and Properdin**] *Ann. Inst. Pasteur*. 1959, Feb., v. 96, No. 2, 178–83, 1 fig.

Properdin is commonly measured by its ability to fix C'3, the 3rd component of complement, in the presence of zymosan. VAN VUNAKIS *et al.* (*Proc. Nat. Acad. Sci.*, 1956, v. 42, 391) have suggested that inactivation of T2 phage by normal serum provides an alternative method of estimating properdin.

The authors have compared properdin levels in normal human sera estimated in these 2 ways. They found no relation between them. [COWAN (this *Bulletin*, 1959, v. 34, 180) has pointed out that the properdin level in normal human serum depends upon the phage used to assay it.] The inactivation of T2 by horse serum has also been measured. The antiphage titres of serum from horses immunized with diphtheria and tetanus toxoids were much lower than those of sera from normal animals. *Janice Taverne*

KUBITSCHEK, H. E. & BENDIGKEIT, H. E. **Delay in the Appearance of Caffeine-Induced T5 Resistance in** *Escherichia coli*. *Genetics*. 1958, Sept., v. 43, No. 5, 647–61, 7 figs. [12 refs.]

MUTSAARS, W. La réactivation multiple du bactériophage inactivé par voie physique et chimique. (Troisième partie.) [**Multiplicity Reactivation of Bacteriophage inactivated by Physical and Chemical Agents**] *Ann. Inst. Pasteur*. 1959, Jan., v. 96, No. 1, 93–105.

Phage N inactivated by formaldehyde was found to yield more plaques upon single infection of *Escherichia coli* W when infection was done at 0°C. than at 37°C. In both cases the number of plaques formed was increased if plates were held at 42°C. for 1½ hours before overnight incubation at 37·5°C.

When phage inactivated by UV irradiation was added at intervals to mixtures of formolised phage and bacteria, fewer plaques were obtained than with formolised phage alone. In contrast, the addition of irradiated phage to phage partially inactivated by ninhydrin increased the number of plaques obtained

[See also this *Bulletin*, 1957, v. 32, 485; 1958, v. 33, 525.] *Janice Taverne*

DROZHEVKINA, M. S. *Brucella* **Bacteriophage and the Prospects of its Utilization.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 9/10, 1221–5. [Translated from Russian.]

This paper summarizes the results of a 7-year study of *Brucella* phages. It is not quantitative and few details are given. The properties of *Brucella* phages appear to resemble those of other phages. Most cultures carry temperate phages and virulent phages are rare. Secondary bacterial colonies growing in areas of lysis are immune to the phage causing the lysis (presumably because they have been lysogenized). More phage is released from lysogenic strains after UV irradiation. Serological differences have been observed between phages. Besides O phages, phages differing in plaque type and which are specific for the Vi antigen have been discovered. [No references are given, but it is possible that this corresponds to the Vi antigen described by WOLFF and DINGER, this *Bulletin*, 1951, v. 26, 949.] *Brucella* species freshly isolated from cases have been quickly and successfully identified by phage typing

Some unusual observations are mentioned. It is reported that when polyvalent *Brucella* phage antiserum was added to plates inoculated with specimens from patients, more positive results were obtained; also, colonies were visible in 2–3 days instead of the usual 7–10 days. *Brucella* phages were commonly isolated from the blood of patients with brucellosis, and in most cases clinical improvement was correlated with a rise in phage titre. In some experiments on the therapeutic effects of *Brucella* phages inoculated into infected guineapigs, it was found that there was a loss of brucellin sensitivity, the agglutinin titre rose more rapidly and the bacteria disappeared more rapidly.

It is recommended that *Brucella* phages and their antisera should be used routinely in the bacteriological diagnosis of brucellosis. *Janice Taverne*

MAMATSASHVILI, E. G. **Some Properties of** *Brucella* **Bacteriophage.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 9/10, 1225–8, 2 figs. [Translated from Russian.]

The author had noticed that changes in the appearances of *Brucella* colonies with time suggested that they were being attacked by a phage. He reports the isolation of phage from many bacterial types, by the (unspecified) technique of Drozhevkina. Phage was also isolated from a live *Brucella* vaccine made from an attenuated strain suspended in fluid, and from a dried live vaccine. Phage was isolated from the faeces, milk and urine of vaccinated cows with a high agglutinin titre. Altogether 53 strains of phage were isolated from 97 experimental sources. Most of the strains of phage acted upon only a few strains of *Brucella*. The author states that classification of *Brucella* strains by phage sensitivity does not fit in with the currently accepted classification since one strain of phage can lyse 2 or even all 3 *Brucella* types. *Janice Taverne*

MACH, F. Morphologie und Wirtsspezifität von Aktinophagen. (Kurze Mitteilung.) [**Morphology and Host Specificity of Actinophages (Brief Communication)**] *Zent. f. Bakt.* II. Abt. 1958, Aug. 30, v. 111, Nos. 16/20, 553–61, 10 figs. [24 refs.]

3 strains of actinophage (AP-1, AP-2 and AP-3) have been isolated from compost and leaf mould and their specificity has been tested on 10 species of *Streptomyces*. The AP-1 strain lysed *Str. coelicolor*, *Str. griseus*, *Str. scabies* and 4 unnamed species, the AP-3 strain lysed the same species except for *Str. coelicolor*, and the AP-2 strain was strictly monovalent, lysing only an unnamed species. The appearance of the phages both lying free and attached to spores of the host organism are shown in electron micrographs, and the following dimensions were observed: AP-1, tail very long, 335–340 mμ in length and 15 mμ in diameter, head 83–85 mμ in diameter, pentagonal, frequently with visible internal structure; AP-2, tail 115–20 mμ × 20 mμ, head electron-dense, 82 mμ, hexagonal; AP-3, tail 275–280 mμ × 22–24 mμ, head 85–90 mμ, with internal granules. *D. J. Bauer*

VIRUSES

In this section the abstracts are arranged as far as possible in the following order:—General; Psittacosis-lymphogranuloma viruses; Pox viruses; Respiratory and other viruses; Enteric viruses; Arthropod-borne viruses; Others.

COOPER, P. D., BURT, A. M. & WILSON, J. N. **Critical Effect of Oxygen Tension on Rate of Growth of Animal Cells in Continuous Suspended Culture.** [Correspondence.] *Nature.* 1958, Nov. 29, v. 182, 1508–9, 1 fig.

The modern virologist requires a regular supply of uniform tissue culture cells. Cell lines which can be propagated indefinitely in the laboratory appear very suitable for much experimental and diagnostic work on viruses and if the possibility of their malignancy could be refuted they would be a great boon for the manufacturer of viral vaccines. These facts have given great impetus to work on the continuous culture of such cells in suspension. This report is a brief description of a successful method of continuous suspended culture of transformed embryo rabbit kidney cells [WESTWOOD *et al.*, this *Bulletin*, 1957, v. 32, 815]. The cells were grown at 37°C. in a 20-litre bottle containing 1·5 litres of culture medium. Medium was pumped in at a known rate and overflowed into another 20-litre container which was cooled to 30°C. The medium was Earle's saline with lactalbumin hydrolysate, amino acids, yeast extract, vitamins, horse and calf serum and 6 to 8 gm. per litre of glucose. The culture vessel was stirred by means of a magnetic stirrer and gassed with carbon dioxide, oxygen and nitrogen. The *p*H of the medium was controlled by varying the carbon dioxide concentration between 2–5%. It was found that the cell growth rate was dependent on oxygen levels. The important factor is the liquid phase oxygen level so the gas phase oxygen level for optimal growth will vary with the cell density and rate of agitation. 25–30% oxygen was found to be rapidly cytocidal whereas when a drop from 19–17% oxygen occurred there was an increased growth rate by 50%.

Using this continuous culture system for 4 months the authors found that the average yield of cells per day was 10^9 in one litre of medium. The mean doubling time was 25 hours but was sometimes 16 hours or less. The harvested cells were used for the growth of polioviruses making 10^{11} to 10^{12} plaque forming units per week. The cells were also used for the agar suspension plaque assay method described by Cooper (*Virology*, 1955, v. 1, 397). *A. J. Beale*

HOANG, T. N., ROHDE, W. & KOTSCHATE, R. **Use of Papain for the Preparation of Monolayer Tissue Cultures.** *Acta Virologica.* Prague. 1959, Jan., v. 3, No. 1, 56–8, 4 figs. on pl.

"It has been found that papain either in the purified or in the crude and dried form could be used for the dissociation of tissue fragments into cell suspensions; the results were as good as those obtained with trypsin.

"The total number of cells released by both forms of papain was at least the same as with trypsin. The cells were able to multiply satisfactorily and could be used for virus cultivation.

"The possibility of using the crude form of papain provides a simple source of enzyme. The time consuming and expensive purification procedure seems therefore not necessary."

HORVÁTH, S. & BALÁZS, V. **A Quantitative Semi-Micro Tissue Culture Method and its Use in Microbiology. I. Quantitative Semi-Micro Tissue Culture Method.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 4, 415–32, 13 figs. [19 refs.]

ROTHBLAT, G. H. & MORTON, H. E. **Detection and Possible Source of Contaminating Pleuropneumonialike Organisms (PPLO) in Cultures of Tissue Cells.** *Proc. Soc. Exper. Biol. & Med.* 1959, Jan., v. 100, No. 1, 87–90, 1 fig. [20 refs.]

"1) A total of 37 tissue cell lines growing in the presence of horse, calf, human, rabbit or dog serum have

been tested for contamination by PPLO. Of these, 22 or 59% contained PPLO. Human, monkey, and mouse cell lines were contaminated. All first and second passages of cell lines were negative. PPLO were isolated from tissue cells growing in human, horse or calf serum. Nineteen positive cell lines were, at some time, grown in presence of human serum. Three positive lines growing in horse serum had never been in contact with human serum. 2) All 25 samples of sera, including pooled lots of human, calf, and horse sera, were negative for PPLO. 3) Possible sources of PPLO contamination of tissue cell cultures are discussed."

COLÓN, J. I. & MOULDER, J. W. **Folic Acid in Purified Preparations of Members of the Psittacosis Group of Micro-Organisms.** *J. Infect. Dis.* 1958, Sept.–Oct., v. 103, No. 2, 109–19, 9 figs. [24 refs.]

The size and complexity, physical and chemical, of the psittacosis-lymphogranuloma group and their susceptibility to a number of chemotherapeutic agents suggest that they possess a number of enzymes, yet only one—cytochrome C reductase—has so far been demonstrated. In the search for other independent enzyme activities in these infective agents the authors of this paper have studied their sulphonamide sensitivity. The work of MORGAN [this *Bulletin*, 1949, v. 24, 94; 1952, v. 27, 894] has shown that this sensitivity is reversed competitively by *p*-aminobenzoic acid (PABA) and non-competitively by pteroylglutamic acid (PGA) as in the case of a bacterium. And since an agent of the psittacosis group can be inhibited by a sulphonamide when growing in a cell, it should be capable of synthesizing folic acid from simpler substances, and this activity is supposed to be essential for multiplication. The formation of folic acid by the agents of psittacosis, meningopneumonitis, feline pneumonitis and mouse pneumonitis when growing in the allantoic cavity has been studied. It has been shown that the virus particles contain folic acid in a concentration comparable to that of chick embryo cells or bacteria. The intrinsic nature of this virus folic acid was supported by the observations:

1. Virus-infected allantoic fluid contained folic acid while the uninfected did not. The folic acid in the infected fluid sedimented with the virus.
2. Each virus presented unique analytical values for folic acid.
3. Alteration of the folic acid content of infected allantoic fluid by the addition of PGA did not increase the virus-associated folic acid.
4. Loss of infectivity of purified virus suspensions is parallelled by a loss in folic acid. *S. P. Bedson*

STEWART, R. B. **The Effect of Cortisone on the Lethality of Psittacosis Virus for the Chick Embryo.** *J. Infect. Dis.* 1958, Sept.–Oct., v. 103, No. 2, 129–34, 1 fig. [13 refs.]

Evidence is produced that cortisone given with psittacosis virus to embryonated eggs by the yolk-sac route delays the death of the embryo. Cortisone is without effect on the virus *in vitro*. The results *in vivo* are the same whether the cortisone is given before, with or 3 hours after, the virus. *S. P. Bedson*

MOULDER, J. W., RUDA, Jacqueline & GREENLAND, Rima M. **Separation of Mixtures of two Drug-Resistant Strains of Feline Pneumonitis Virus by limiting Dilution Passage in Chick Embryo Yolk Sac.** *J. Infect. Dis.* 1958, Sept.–Oct., v. 103, No. 2, 172–7. [17 refs.]

Making use of 2 strains of feline pneumonitis virus, one penicillin-sensitive and the other sensitive to quinoxaline oxide, the authors produce evidence that clones of the psittacosis group of infective agents can be obtained by passage in the chick embryo yolk sac at limiting dilutions. As previously found with this method, it is necessary to use inocula giving a very low rate of infection, to isolate a number of presumptive clones from each population and if necessary, to repeat passage at limiting dilutions. *S. P. Bedson*

NISHMI, M. & BERNKOPF, H. **The Toxic Effect of Vaccinia Virus on Leucocytes** *in vitro*. *J. Immunology*. 1958, Dec., v. 81, No. 6, 460–66, 4 figs. [20 refs.]

The authors showed that fairly heavy doses of vaccinia virus (with infectivity titres 10^6/ml.) were able to induce cytopathic changes in both human leucocytes and white cells obtained from peritoneal exudates of mice. The destruction of cells observed was not associated with virus multiplication, but was completely inhibited by a specific anti-vaccinial serum. The authors consider this to be a toxicity phenomenon. Reduction of infectivity 200-fold by heating a virus preparation reduced its toxicity by 20-fold. A 300-fold reduction of infectivity by ultraviolet irradiation was accompanied by a 3-fold reduction in toxicity. Toxicity could not be separated, by centrifugation, from virus particles.
Colin Kaplan

BUKRINSKAYA, A. G. **Type D Influenza Virus Cultivation in Human Embryonic Tissues.** *Acta Virologica*. Prague. 1958, Oct.–Dec., v. 2, No. 4, 208–19, 4 figs. [13 refs.]

Influenza D virus (Sendai virus, haemagglutinating virus of Japan, newborn pneumonitis virus) was found to multiply, reaching high titres and causing cytopathic effect in cultures of human embryonic lung and tongue and monkey kidney tissues. Multiplication without cytopathic effect was observed in cultures of human embryonic kidney and chick embryonic lung. No multiplication could be detected in embryonic human and chick muscle or in HeLa cells. The rate of virus multiplication and haemagglutinin production in cultures of human embryonic lung is presented. Evidence is presented suggesting that virus multiplication may be inhibited by antibiotics of the tetracycline group.
H. G. Pereira

FABIYI, A.; LIEF, Florence S.; HENLE, W.; OSTAPIAK, M. **Antigenic Analysis of Influenza Viruses by Complement Fixation. II. The Production of Antisera to Strain-Specific V Antigens in Guinea Pigs** [FABIYI, LIEF & HENLE]. *J. Immunology.* 1958, Dec., v. 81, No. 6, 467–77, 2 figs. [25 refs.] **III. Rapid Identification of New Isolates** [LIEF, OSTAPIAK, FABIYI & HENLE]. *Ibid.*, 478–83. [18 refs.]

II. The antigenic constitution of 34 strains of influenza A virus isolated between 1931 and 1957 was studied by means of complement-fixation tests. The strain and type specificity of virus (V) and soluble (S) antigens is discussed and methods for obtaining strain specific V antigens and the corresponding anti-V sera are described. Absence of S component from the V antigens was checked by tests performed against highly active anti-S sera. Reactions between V antigens and anti-V sera gave strain-specific results allowing the distribution of the strains under study into 4 groups representing the Swine, A, A-prime and Asian families of influenza A. Cross-reactions between strains of different families were frequently observed but the heterologous titres were always lower than the homologous. It is suggested that the heterologous reactions are due to minor antigenic components shared by different strains. Non-reciprocal cross-reactions were also observed and are assumed to indicate the presence of minimal amounts of antigen which can only be detected by their capacity to stimulate antibody production.

III. Influenza viruses isolated in the course of 2 separate outbreaks in 1957 were identified by means of complement-fixation tests with strain-specific virus (V) antisera free of antibodies for the type specific soluble (S) antigen. 3 strains isolated during the first outbreak were shown to belong to the A-prime family and to be closely related to but not identical with the Nederland 36 strain isolated in 1956. A detailed study of the antigenic constitution of the virus isolates was carried out with antisera prepared against the new strains. Asian strains isolated during the second outbreak were readily identified by the methods described. Of 51 viruses obtained from throat washings, 80% were diagnosed on first egg passage. Egg fluids with haemagglutination titres as low as 20 to 40 units per ml. could be used as complement-fixing antigens. Presence of S antigen in the egg fluids did not interfere with the strain specificity of the results as the sera employed were free of S antibodies.

Advantages of complement-fixation over haemagglutination-inhibition tests are discussed.

H. G. Pereira

CULVER, J. O., LENNETTE, E. H., NAVARRE, G. & DONAHUE, Gwendolyn A. **The Recall Phenomenon in the Antibody Response to Influenza Vaccines.** *J. Immunology.* 1958, Dec., v. 81, No. 6, 452–9. [27 refs.]

Antibody responses to a formalin-inactivated influenza vaccine containing A-prime strains FMI and Cuppett were investigated by serological tests performed in sera from vaccinated and control subjects. Pre- and post-vaccination sera were tested by complement-fixation and haemagglutination-inhibition against PR8, FMI and Cuppett antigens. Complement-fixing titres for the PR8 antigen rose more frequently and to higher levels than those for the A-prime strains contained in the vaccine. An inverse relationship between pre-vaccination antibody level and post-vaccination antibody response was observed. It is suggested that the higher reactivity of post-vaccination sera with PR8 antigen may be due to a recall phenomenon stimulated by minor antigenic components shared by A and A-prime influenza viruses. [See also HENLE, LIEF and FABIYI, this *Bulletin*, 1958, v. 33, 710.] *H. G. Pereira*

BOGERT, A. B. & CORBETT, J. J. **The Quantitative Effects of Cations on Erythrocyte Agglutination by Influenza Virus Vaccine.** *J. Immunology.* 1958, Dec., v. 81, No. 6, 524–6, 1 fig.

Variations in haemagglutination titres given by influenza vaccines were correlated with the batches of distilled water used for the preparation of saline and buffer solutions employed in the tests. The factor responsible for this variation was found to be the concentration of metal ions in the water. Haemagglutination titres were either increased or reduced according to total and relative concentration of metal ions in given combinations. *H. G. Pereira*

KILBOURNE, E. D. **Inhibition of Influenza Virus Multiplication with a Glucose Antimetabolite (2-Deoxy-D-Glucose).** [Correspondence.] *Nature.* 1959, Jan. 24, v. 183, 271–2, 1 fig.

The importance of the endogenous glucose in *in vivo* multiplication of influenza virus was studied by testing the action of the glucose antimetabolite 2-deoxy-D-glucose on virus production in the allantoic cavity of fertile eggs. Eggs receiving 12·5 or 25·0 mgm. of 2-deoxy-D-glucose 18 hours before inoculation with a large virus dose were compared with control eggs by haemagglutinin titrations performed after 8- and 24-hour periods of virus multiplication. Nearly maximal titres were reached in control eggs at 8 hours, when the titres in eggs injected with 2-deoxy-D-glucose were 8 to 32 times lower. No significant titre differences were found at 24 hours' incubation. Injection of 50–250 mgm. of glucose did not prevent or reverse the *in vivo* effect of 2-deoxy-D-glucose. This effect was, however, inhibited by pyruvate [this *Bulletin*, 1957, v. 32, 382.] *H. G. Pereira*

SUTTON, R. N. P., CLARKE, Suzanne K. R. & TYRRELL, D. A. J. **Newly Recognised Myxoviruses in Europe.** *Lancet.* 1959, Feb. 21, 395.

CHANOCK *et al.* in the United States [this *Bulletin*, 1958, v. 33, 621] isolated 2 new viruses from children with respiratory disease, naming them HA1 and HA2. A virus serologically identical with HA1 has now been isolated from a child in Sheffield, and the authors also show that the virus isolated from a child in Copenhagen by PETERSEN and VON MAGNUS [*ibid.*, 995] is identical with HA2.

These are the first strains of HA1 and HA2 to be isolated in Europe. *Charles Wilcocks*

ODDO, F. G. L'evoluzione dell'infezione di cellule HeLa con virus poliomielitico, studiata attraverso le alterazioni morfologiche e la dimostrazione di antigene virale a mezzo di anticorpi fluorescenti. [**The Course of Development of Infection of HeLa cells with Poliomyelitis Virus as studied by Morphological Changes and the Demonstration of the Virus Antigen by Fluorescent Antibody**] *Giorn. di Microbiol.* Naples. 1957, Nov.–Dec., v. 4, No. 3, 153–65, 2 graphs & 19 figs. on 7 pls. [20 refs.] English summary.

HeLa cells infected with the Brunhilde strain of poliomyelitis virus were examined by the fluorescent antibody technique at intervals after infection; up to 3 hours the cells showed only unspecific fluorescence, but in cultures examined after 3½ hours specific fluorescence was observed in 40% of the cells, and after 5 hours the proportion had risen to 82%. The specific fluorescence was confined to the cytoplasm; it was usually diffuse, and declined in intensity towards the periphery of the cell, although fluorescent granules were sometimes observed. Cells examined after 5 hours had become rounded, and the nuclei were still devoid of antigen. In cells fixed and stained with Giemsa after 3 hours changes were beginning to appear in the nuclei, which were reduced in volume and irregular in outline, with alteration of structure in the chromatin reticulum. Titrations of cultures disrupted by sonic vibration showed that new virus began to appear after 3 hours, synchronously with the appearance of antigen and the development of nuclear changes.

D. J. Bauer

KANDA, Y. & MELNICK, J. L. *In vitro* **Differentiation of Virulent and Attenuated Polioviruses by their Growth Characteristics on MS Cells.** *J. Exper. Med.* 1959, Jan. 1, v. 109, No. 1, 9–24, 5 text figs. & 5 figs. on 3 pls. [17 refs.]

Poliovirus strains possessing the d character (delayed or inhibited plaque formation under low bicarbonate containing agar) have been found to be of low pathogenicity for monkeys [VOGT *et al.*, this *Bulletin*, 1958, v. 33, 891 *bis*]. The correlation between d character and attenuation is not perfect, some strains have reverted to d+ but remained avirulent. It has now been found that several virulent strains of poliovirus produce large plaques (4–5 mm.) on MS strain of monkey kidney cells (MS+), whereas attenuated strains produce very small or no plaques on this cell strain (MS character). Attenuated viruses also produce less virus in this cell strain than virulent strains.

The most virulent strains are MS+ and d+, and the most attenuated MS d, whereas strains classified as MS d+ are partially attenuated. In the neuropathogenicity tests an attenuated strain was arbitrarily chosen as one that did not produce paralysis with a dose of 10^5 PFU (plaque forming units) inoculated intracerebrally.

The Saukett Type 3 strain incorporated in killed poliovaccine was MS d+ and partially attenuated (*i.e.* mild central nervous system lesions but no paralysis after intracerebral inoculation). 16 freshly isolated strains of Type 3 poliovirus were examined (8 from paralytic cases and 8 from non-paralytic cases) for MS and d characters. All 8 of those from non-paralytic poliomyelitis and 4 from paralysed patients were MS d+ and the remainder MS+ d+. 1 of the MS+ d+ strains was virulent for monkeys and 1 MS d+ strain was avirulent.

It is suggested that work on *in vitro* markers correlated with attenuation are urgently required in order to test the virulence of strains of poliovirus excreted by the increasing number of people being given attenuated poliovaccines.

[Adequate methods of testing the virulence of virus excreted from individuals given attenuated poliovaccine are urgently required. It seems that these excreted strains should be shown to be attenuated before mass use of attenuated poliovaccine is warranted, at least in areas where poliovirus immunity is sufficiently low to allow epidemics of poliomyelitis to occur.]

A. J. Beale

GARD, S., with the technical assistance of Eva HERRSTRÖM & Karin HOLMGARD. **Further Studies on the Use of Guinea Pigs in Tests for Immunogenic Capacity of Poliovirus Preparations.** *Arch. f.d. gesamte Virusforschung.* 1958, v. 8, No. 4, 411–22, 4 figs. [11 refs.]

Gard has previously described an antigenic extinction titre method of assaying potency of inactive or active poliovirus preparations with guineapigs [this *Bulletin*, 1956, v. 31, 757]. Although he considers this method to be the best now in use it has a standard error of about 0·3 log units [MELÉN *et al.*, *ibid.*, 1957, v. 32, 1115] and is not sufficiently accurate for controlling poliovaccine production. Recently Gard described a new method, immuno-inactivation, of titrating serum neutralizing antibodies which is more sensitive than those at present in use. By means of this method the response of guineapigs to living and inactivated poliovirus was studied. It was assumed that after a single primary dose of poliovirus antigen the peak titres were reached at 7 days. It was found that during the period 7–21 days the antibody titre fell rapidly with a half life of 2½ days.

Provided a sufficient primary stimulus was given a state of hyper-reactivity was induced to a second dose. The degree of hyper-reactivity was not related to the amount of antigen given in the first dose, it was an all or none phenomenon, but the duration of the hyper-reactive state was influenced by the potency of the primary stimulus. The primary antigen dose was not linearly related to the mean antibody response except over a narrow range (less than 10-fold) near the minimum dose eliciting any response at all. Over this range, however, the accuracy of the test was not high. The results of a few observations suggest that there may be a straight line relationship between antigen dose used to elicit the secondary response and the mean titre obtained. This appeared to hold good over a 1,000-fold range of antigen dose.

Gard is now trying out a test for potency in which presensitized guineapigs are used (they are given $10^{6\cdot2}$

TCD50 of live virus at least 6 weeks before use) and the response is measured to dilutions of the preparation under examination. *A. J. Beale*

GARD, S., JOHNSON, T., LYCKE, E., MELÉN, B., OLIN, G., SALENSTEDT, R. & WRANGE, G. **Potency of Inactivated Poliovirus Vaccines. Correlation between Antigenic Extinction Limit Titers in Guinea Pigs and Results obtained in Man.** *Arch. f.d. gesamte Virusforschung.* 1958, v. 8, No. 4, 423–9, 1 fig.

The potency of 4 poliovaccines was determined by the antigen extinction technique with guineapigs [GARD *et al.*, this *Bulletin*, 1956, v. 31, 757] and was compared with the response in triple negative children. For 2 vaccines antigen extinction titres were determined in children and it was found that for Types 1 and 3 the titre was about a log higher with guineapigs, whereas there was less difference in the titres for Type 2. The great majority of triple negative children responded to the Type 2 component of all 4 vaccines. The response to Types 1 and 3 was poor except for one vaccine preparation which also had the highest antigen extinction titre in guineapigs. It was estimated that vaccines with the following antigen extinction titres will produce a response in 80% of triple negative children: Type 1, $10^{-1.91}$; Type 2, $10^{-0.88}$; Type 3, $10^{-2.1}$. Only 1 of 4 vaccines reached this standard with titres of $10^{-2.08}$, $10^{-2.50}$ and $10^{-2.43}$ to Types 1, 2 and 3 respectively. *A. J. Beale*

DE SOMER, P., DE MAEYER, E. & PRINZIE, A. **A Four Point Assay for testing Poliovaccine.** *Arch. f.d. gesamte Virusforschung.* 1958, v. 8, No. 4, 430–36, 3 figs. [13 refs.]

There is as yet no adequate test for poliovaccine potency. The most accurate method at present described is the antigen extinction method with guineapigs [GARD *et al.*, this *Bulletin*, 1956, v. 31, 757] which can just distinguish 10-fold differences. A new more accurate test with chicks is proposed. This is based on the observation that the geometric mean $\log_2$ antibody titre is linearly related to the log vaccine dose with 3-week-old chicks bled 7 days after a single dose. The slope of this straight line was found to be 0·74. In order to compare 2 vaccines 2 dilutions of each are tested with 30 chicks per test. It was calculated that the standard deviation of such a test is just over 0·1 $\log_{10}$ unit, *i.e.* that 3-fold differences in potency are detectable. This method should be used with a preparation of standard potency, but such a standard and its conditions of storage is not yet established. By means of this method it was found that the loss of potency at 24°C. was appreciable from which it was implied that the decline at 4°C. would also not be negligible. After 30 days at 24°C. 30% of the Type 2 and 3 potency remained and 15% of the Type 1. At 37°C. the decline in potency was faster reaching 30% for Type 1 in about 15 days.

[This interesting paper presents very few details for the reader to assess the results for himself.]

A. J. Beale

KASEL, J. A., CRAMBLETT, H. G. & UTZ, J. P. **Agents resembling Enteroviruses isolated in HeLa Cell Cultures from Fecal Specimens.** *Proc. Soc. Exper. Biol. & Med.* 1958, Dec., v. 99, No. 3, 703–5.

8 viruses were isolated from faeces of 10 patients with respiratory illness in Washington. Virus was not isolated from pharyngeal conjunctival or nasal swabs. The viruses failed to produce cytopathic effects in monkey kidney cells or clinical effects in suckling mice. The viruses produced cytopathic effects in HeLa cells (and a wide variety of other "epithelial" cell lines) like those produced by poliovirus. They also produced cytopathic effects but more slowly in a strain of human embryonic fibroblasts (MAF). The agents were not pathogenic for a wide variety of laboratory animals nor chick embryos. They did not agglutinate human, chick or guineapig (less than 3 days old) red cells. They were not destroyed by ether. The viruses seemed to fall into the enterovirus family but an antiserum against the prototype strain (Pett) did not neutralize any member of the family tested, Coxsackie A 1–19, B 1–5, ECHO 1–20 and poliovirus 1–3. Satisfactory neutralization tests with the new agents could only be done in MAF cells. All the viruses seemed closely related and paired sera from 5 of the patients showed a rise in neutralizing antibodies. *A. J. Beale*

POLJAK, V. & BÁRDOS, V. Laboratorní nákaza virusem lymfocytární choriomeningitidy. **[Laboratory Infection with Lymphocytic Choriomeningitis Virus]** *Časopis Lékařů Českých.* Prague. 1958, Sept. 19, v. 97, No. 38, 1185–91, 1 fig. [Numerous refs.] English summary.

The authors describe the first instance of a laboratory infection with lymphocytic choriomeningitis reported in Czechoslovakia. The patient was a female laboratory assistant aged 35 who had carried out autopsies on mice infected with various viruses. The onset was acute, with frontal headache, rigors, a temperature of 38°C. and meningism. By the 5th day the temperature fell to normal, but the patient suffered from persistent vomiting. After an afebrile interval of 4 days the temperature again rose to 38°C., with continual vomiting, pain in the abdomen and limbs and severe headache. Recovery set in on the 18th day and the patient was discharged in good condition on the 31st day of illness. Blood taken on the 3rd day of illness was inoculated into mice intracerebrally and a strain of virus was recovered which was identified as lymphocytic choriomeningitis by cross-protection tests in mice. Complement-fixing and neutralizing antibodies to the same virus could be demonstrated in rising titres in sera taken from the patient between the 4th and 18th days of illness. *D. J. Bauer*

PRIMAVESI, K. A. & STÖCKER, E. M. Untersuchungen zum Nachweis des Hepatitis-Virus im Mäuseversuch. **[Investigations on the Detection of Hepatitis Virus in Experiments in Mice]** *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 2, 181–98, 7 figs. [Numerous refs.]

In attempts to infect mice with infective hepatitis virus duodenal juice from 34 patients suffering from the disease was administered by various routes, and 31 days later the animals were killed and histological examinations were made of the liver. Including control groups 840 mice were used in all. Marked pathological changes were observed in the livers of both treated and control animals, including fatty degeneration, infiltration and acute necrosis. In no case was the appearance typical of infective hepatitis reproduced exactly. The authors conclude that no evidence of adaptation of the virus had been obtained, and stress the possibilities of drawing false conclusions in experiments with mice

D. J. Bauer

BECH, V. **Canine Hepatitis Virus: Attempts to find Relationship with Human Hepatitis.** *Proc. Soc. Exper. Biol. & Med.* 1959, Jan., v. 100, No. 1, 135–7. [18 refs.]

"1) Observations on growth and behavior of a strain of canine hepatitis virus in various tissue culture systems of human and animal origins have been described. 2) By testing acute and convalescent phase sera from human hepatitis patients against canine hepatitis virus in neutralization, complement fixation, and hemagglutination inhibitions tests, no antigenic relationship could be demonstrated between this virus and the infectious agent of human hepatitis."

LEE, H. W., HINZ., R. W. & SCHERER, W. F. **Porcine Kidney Cell Cultures for Propagation and Assay of Japanese Encephalitis Virus.** *Proc. Soc. Exper. Biol. & Med.* 1958, Dec., v. 99, No. 3, 579–83, 4 figs. [15 refs.]

Trypsinized pig kidney (PK) cells were grown in tubes. Foetal kidneys were better than adult. 4 recently isolated strains of Japanese encephalitis virus caused cytopathogenic effects in 2–5 days compared with 6–10 days for high passage Nakayama strain. In serial passage, titres of 10^{-5} to 10^{-8} were maintained. Early passage tissue culture material gave higher titre in mice than in cultures but after the 5th passage the titres were equal. The PK system was found satisfactory for neutralization tests. Maximum virus titres were attained in 3–5 days with 2 of the recently isolated strains.

G. E. Gordon Smith

OKUNO, T., OKUMA, M., NOMURA, S. & KITAOKA, M. **An Evaluation of the Plate Complement Fixation Test with Japanese B Encephalitis and Polio Viruses.** *Japanese J. Med. Sci. & Biol.* 1958, Aug., v. 11, No. 4, 259–75, 5 figs. [20 refs.]

This is an account of the use of the technique described by KRAFT and MELNICK [this *Bulletin*, 1951, v. 26, 189] with only minor modification of the method of complement titration. The Japanese encephalitis antigen was prepared from mouse brain by freezing and thawing [*ibid.*, 1948, v. 23, 76] and HeLa cell culture fluids were used for the poliovirus. Complement was titrated in the presence of antigen both by immediate addition of the haemolytic system and after overnight incubation in the cold. From the immediate titration the lowest dilution causing slight haemolysis was "1 minimal unit" while the highest dilution causing complete haemolysis in the overnight titration was "2 conventional units". The "coefficient of conventional unit" was the ratio: 1 minimal unit to 1 conventional unit. A high coefficient indicated that more complement was needed in the test [but the exact method of calculation is not clear].

Tests with total drop-volumes of 0·2 ml. instead of 0·1 ml. gave similar results. Complement was found to be stable on the plates for at least 27 hours at 4°C. Japanese encephalitis antigens showed little anticomplementary activity after either long or short fixation periods but the poliovirus antigens were markedly anticomplementary after long but not short fixation. This difference was not found with tests done in tubes. 3 units of complement were found to give results corresponding most closely with a conventional test done in tubes. The duration of incubation after addition of the haemolytic system was critical. Analysis of variance applied to a series of tests with both types of antigen showed that results of replicates were usually within 15% of their mean.

C. E. Gordon Smith

AITKEN, T. H. G., DOWNS, W. G. & ANDERSON, C. R. **Parasitic *Philornis* Flies as possible Sources of Arbor Virus Infections (Diptera, Anthomyidae).** *Proc. Soc. Exper. Biol. & Med.* 1958, Dec., v. 99, No. 3, 635–7.

Nestling birds in Trinidad are commonly infested with larval *Philornis* flies of a number of species. One species, of which the larvae feed by rasping the skin and ingesting the exudate, was shown to become infected with St. Louis virus when fed on a viraemic bird and subsequently ground up and inoculated into mice. With another species in which the larvae are subcutaneous, larvae were inoculated with Ilhéus virus: 10–11 days later, 2 of 8 adult flies which had emerged were found to have 20-fold and 50,000-fold increases in virus content compared with the inoculum. Larvae of a coprophilous species were inoculated with St. Louis virus and 9–10 days later 6 of 8 adult flies were found to have 825-fold to more than 137,500-fold increases in virus content. The adult flies do not ingest blood and each single generation of larvae is confined to a single nest so that these infections may have no epidemiological significance unless transovarial infection occurs and birds can be infected by ingestion of the flies. These possibilities have not yet been investigated.

C. E. Gordon Smith

THOMAS, L. A., EKLUND, C. M. & RUSH, W. A. **Susceptibility of Garter Snakes (*Thamnophis* Spp.) to Western Equine Encephalomyelitis Virus.** *Proc. Soc. Exper. Biol. & Med.* 1958, Dec., v. 99, No. 3, 698–700.

The overwintering of western equine encephalomyelitis in the United States is still inadequately explained. The vector *Culex tarsalis* was observed to hibernate in rock piles in which snakes also commonly winter. *C. tarsalis* will bite garter snakes in the absence

of other hosts. *C. tarsalis* were infected with low-passage western equine virus by feeding on viraemic chicks. After the extrinsic incubation period, groups of 2, 9 and 20 mosquitoes were fed on garter snakes (*Thamnophis* spp.). Viraemia was detected in them from 3 to 16, 4 to 23 and 4 to 7 days after being bitten, with maximum titres of 10^{-6}, 10^{-2} and 10^{-3} respectively. Similar results were obtained when snakes were inoculated intraperitoneally.

C. E. Gordon Smith

Von Zeipel, G. & Svedmyr, A. **Growth of Viruses of the Russian Spring-Summer Louping-Ill Group in Tissue Culture.** *Arch. f.d. gesamte Virusforschung.* 1958, v. 8, No. 3, 370–84, 3 figs. [31 refs.]

A strain of louping ill virus adapted to HeLa cells was compared with a mouse-brain strain in HeLa and Detroit-6 cells. The Detroit-6 cells were superior to the HeLa cells and gave titres as high as in mice. Louping ill virus was also tested for cytopathogenicity in human amnion, human kidney and monkey kidney but none was detected. Czech strains of tick-borne encephalitis gave lower titres in Detroit-6 cells than in mice. Neutralization tests comparing acute and convalescent phase sera from cases of tick-borne encephalitis demonstrated rises in antibody titre from 2·5- to 12-fold depending on the time and temperature of incubation of serum-virus mixtures and on the virus dosage. Cross-neutralization tests between louping ill and tick-borne encephalitis viruses revealed some antigenic difference. Fluids from flask cultures of Detroit-6 cells infected with virus could be used as complement-fixing antigens but were anticomplementary unless 5–10% of inactivated guineapig serum [this *Bulletin*, 1958, v. 33, 1095] was incorporated in the medium. In tests with acute and convalescent sera differences were found between louping ill and tick-borne encephalitis antigens, the latter giving higher titres and more responses with Swedish sera. Heating the antigens at 56°C. for 30 minutes destroyed the antigens but treatment with ultraviolet light or β-propiolactone [*ibid.*, 1956, v. 31, 469; 1957, v. 32, 1117] appeared to be capable of destroying infectivity without significant loss of antigenicity. *C. E. Gordon Smith*

De Ruyck, R. & Lépine, P. Effets pathogènes du virus choriotrope en culture de tissus. [**The Pathogenic Effects of Choriotropic Virus in Tissue Culture**] *C.R. Soc. Biol.* 1958, v. 152, No. 3, 448–9.

It has previously been claimed that a virus can be isolated from hydatidiform mole and chorion epithelioma and cultivated in chick embryo tissue with the production of a cytopathogenic effect [De Ruyck, *Bull. Ass. Française Cancer*, 1951, v. 38, 52, 252; 1953, v. 40, 78; 1957, v. 44, 205; De Ruyck and Lépine, *C.R. Soc. Biol.*, 1956, v. 150, 664]. In the present work an account is given of the behaviour of the virus (choriotropic virus) in cultures of trypsinized chick embryo liver cells. After 10–12 days the fibroblasts of cultures derived from 9-day-old embryos become transformed into large syncytia containing up to 150 nuclei, with vacuolated cytoplasm containing inclusions. Other fibroblasts remain of normal size but contain groups of metachromatic cytoplasmic granules. In cultures derived from 19-day-old embryos the liver epithelial cells are mainly affected, enlarging greatly and anastomozing, with metachromatic inclusions which are sometimes excreted and surround the cells. The syncytia which are formed have an appearance similar to those characteristic of chorionepithelioma.

D. J. Bauer

IMMUNITY

Steigman, A. J. & Lipton, M. M. **Neonatal Immunity. II. Poliocidal Effects of Human Amniotic Fluids.** *Proc. Soc. Exper. Biol. & Med.* 1958, Dec., v. 99, No. 3, 576–9.

Brambell *et al.* [this *Bulletin*, 1954, v. 29, 892] have shown that in the rabbit maternal antibodies reach the young by way of the amniotic fluid. Amniotic fluid, maternal and cord serum were collected from 22 women at the time of delivery. A heat-labile poliovirus inhibitor substance was present in many amniotic fluids as well as substances that appeared to be specific poliovirus neutralizing antibody. Thus the substance, thought to be antibody, was present in a roughly constant ratio to the maternal and cord antibody titre (around 1:64). Amniotic fluid contains gamma globulin and in one experiment a 10-fold concentration of gamma globulin (achieved by ammonium in sulphate precipitation) led to a roughly equal concentration of gamma globulin measured immunologically and of the 3 types of poliovirus antibodies.

[For Part I see *ibid.*, 1958, v. 33, 320.] *A. J. Beale*

Becker, E. L. **Concerning the Mechanism of Complement Action. IV. The Properties of Activated First Component of Guinea Pig Complement.** *J. Immunology.* 1959, Jan., v. 82, No. 1, 43–51, 3 figs. [16 refs.]

"C′1 and TAMe esterase activity can be eluted from sensitized sheep red cells containing C′1 activity by ethylenediaminetetraacetic acid. On dialyzing the supernatant from cells so treated against a low ionic strength buffer, both activities can be recovered. The C′1 activity eluted from red cells in this fashion can be detected with ease by a two-step procedure of adding the "eluate" to sensitized cells, washing and then adding an R1. If an R1, sensitized cells and the "eluate" are added together little or no evidence for C′1 activity is obtained. The properties of the enzyme when removed from the cell are the same so far as studied as when the enzyme is attached to the cell. When sensitized cells are treated with the eluate not only does C′1 activity attach itself to the cells but esterase activity as well. Allowing the eluate to stand in the cold at pH 3·3, affects its TAMe esterase activity little if at all; however, the C′1 activity and the ability

of the esterase to attach to sensitized cells is destroyed and, as kinetic studies showed, destroyed to the same extent. In explanation of these latter observations the hypothesis was evoked that the C'1 molecule contains two distinct sites, a binding site and an enzymatic site, and both are required in order for the molecule to manifest C'1 activity."

WEDGWOOD, R. J. **Concerning the Nature of the Properdin System.** *Pediatrics.* Springfield, Ill. 1958, Nov., v. 22, No. 5, 991–1000. [70 refs.]

Publications on the properdin system have multiplied steadily during the 5 years since it was first described. This review gives an adequate and critical description of the published work. The author's conclusion that "It seems improbable that a system with such diverse activities would exist without a biologic function in vivo, but such a function has yet to be demonstrated" is a fair statement of our present knowledge of the role of properdin in nature. *R. B. Morrison*

HUMPHREY, J. H. & MOTA, I. **The Mechanism of Anaphylaxis: Observations on the Failure of Antibodies from Certain Species to sensitize Guinea Pigs in Direct and Reversed Passive Anaphylaxis.** *Immunology.* Oxford. 1959, Jan., v. 2, No. 1, 19–30, 2 figs. [21 refs.]

"Using the criteria of generalized anaphylaxis, the Schultz-Dale test, and mast cell degranulation occurring on contact with antigen *in vitro*, a study has been made of the ability of antisera, prepared in various species, to sensitize guinea pig tissues passively. Whereas small amounts of guinea pig and rabbit antibodies and rather larger amounts of monkey, dog and human antibodies were effective, antibodies from goat, horse, rat, fowl and a human auto-immune thyroid antiserum were ineffective. These results are in general agreement with those in the literature.

"Using antibodies labelled with ^{131}I, no gross differences were found between those which sensitized and those which did not, either in respect of uptake on guinea pig mesentery *in vitro*, or retention in the tissue after uptake *in vivo*. By means of antigen labelled with ^{131}I it was also shown that the antibody adsorbed on guinea pig mesentery could combine equally well with antigen, whether the antibody came from rabbit (sensitizing) or rat (non-sensitizing). These experiments also indicated that the amount of adsorbed antibody necessary for sensitization is very small.

"Reversed passive anaphylaxis was studied with a variety of different antigen-antibody systems, using the criteria listed above. It occurred when, but only when, the antigen was a γ-globulin, and when both antigen and antibody globulins came from species whose antibodies were able to sensitize guinea pigs for direct passive anaphylaxis.

"It is concluded that the explanation of the differences between antibodies or antigens which sensitize guinea pigs passively, and those which do not, is to be found in the nature of the antigen-antibody combination as well as in the manner of 'fixation' on the tissues. The possible importance of ability to activate guinea pig complement is discussed."

HUMPHREY, J. H. & MOTA, I. **The Mechanism of Anaphylaxis: Specificity of Antigen-Induced Mast Cell Damage in Anaphylaxis in the Guinea Pig.** *Immunology.* Oxford. 1959, Jan., v. 2, No. 1, 31–43, 3 figs. [38 refs.]

"Mast cell damage, characterized by loss of granules, occurs when the tissues of sensitized guinea pigs are brought into contact with antigen *in vivo* or *in vitro*. Quantitative studies on the mesenteries of passively sensitized guinea pigs show that the mast cell response to antigen is well correlated with the development of anaphylactic shock. After multiple sensitization contact with different antigens caused cumulative, but not complete, disappearance of mast cells.

"Antigen-antibody interactions, in which antisera were from species which do not sensitize guinea pigs passively for anaphylaxis, did not cause mast cell damage.

"Reversed passive anaphylaxis and mast cell damage were elicited when the antigen was a suitable γ-globulin, but not an albumin. Antiserum against homologous γ-globulin causes typical anaphylaxis and mast cell degranulation, whereas antiserum against Forssman antigen causes capillary damage without mast cell changes, and antiserum against homologous albumin is ineffective.

"These findings can be explained by the hypothesis that mast cell damage occurs as a result of antigen-antibody interaction, when one of the reagents is reversibly adsorbed at the mast cell surface, and when they are together capable of activating some process or agent whose further action depends upon the metabolic integrity of the cells."

Book Reviews

COMMISSION ON CHRONIC ILLNESS [MAYO, Leonard W., Chairman]. **Chronic Illness in the United States. Vol. IV. Chronic Illness in a Large City.** The Baltimore Study. pp. xxii + 620, illustrated. 1957. Cambridge: Harvard University Press, Mass., U.S.A.

This final report in the Commission's series is a companion to Volume III, *Chronic Illness in a Rural Area*, which studied the situation in the Hunterdon County, New Jersey. The large city is Baltimore whose Eastern Health Districts were the site of extensive morbidity studies in 1938–43. This report can be considered the most recent in a long series starting with the Hagerstown Morbidity Studies 30 years previously. It breaks new ground in trying to establish a proper base line for such studies, in estimating the degree of chronic illness not reported by the customary household interview techniques.

The study was divided into 4 phases, (1) Household Interview Study, (2) Clinical Evaluation, (3) Screening and (4) Vocational Rehabilitation Demonstration. For the Household Interview a 1 in 80 sample of addresses, excluding institutions, was obtained giving 3,828 households with about 12,000 people. Interviews began in September 1953 and were completed one year later in nearly 98% of this sample.

Approximately 10% of the basic survey group of 12,000 were chosen for the next phase, Clinical Evaluation, an intensive examination carried out at the Johns Hopkins Hospital about 2 months after the Household Interview. The actual sampling fraction varied with the degree of disability previously reported, from 100% in those with maximum disability to 6% in those reporting no disease. Only 809 of the 1,292 selected for evaluation participated, a response rate of 63%.

The members of sample households not selected for Clinical Evaluation who were over 16 years of age, about 7,000 in total, were invited to the Screening phase, in which a number of tests were applied—height, weight, urinalysis, blood pressure, ECG, chest X-ray, blood sugar, serological tests for syphilis, visual and auditory acuity and dental examination. The response was poorer than expected, only 2,000, 29% of those invited, presenting themselves for interview.

The Vocational Rehabilitation Demonstration was based on the 36 patients who were considered capable of rehabilitation for remunerative employment by the team of doctors and social workers responsible for the Clinical Evaluation. Attempts were to be made to see how far these chronically ill persons could be restored to useful activity; this phase is still continuing.

The Clinical Evaluation revealed an astounding prevalence of 1,600 chronic conditions diagnosed per 1,000 population, and contrary to expectation arthritis, with a rate of 75 per 1,000, was not the most common condition, but was third to mental disease, 109 per 1,000 and heart disease 96 per 1,000. The rates for all chronic diseases increased sharply with age and at most ages were greater for women than men. The differences between white and non-white groups were small and were not consistent at each age. The prevalence rates were, in general, highest in the lowest income groups. Detailed analyses of this type are presented for the specific diagnoses, heart disease, and hypertension, diabetes mellitus, neoplasms, arthritis, mental disorders and syphilis.

The prevalence rate obtained in the Clinical Evaluation was 8 times as great as the rate obtained in the study in the Eastern Health Districts of the same city in 1938–43. Furthermore, less than a quarter of the conditions discovered at the Clinical Evaluation were reported at the preceding Interview. Only one-eighth of the conditions discovered were considered severe, and under-reporting is understandable in mild conditions causing no disability. Nevertheless, reporting was little better for severe conditions, and this raises serious doubts on the validity of rates obtained from household interview procedures.

It was estimated that without care 4 out of the 10 conditions diagnosed would be progressive, while with recommended care only 1 in 7 would continue to progress. One of the major obstacles to applying therapeutic measures was the attitude of the patients themselves.

The volume gives detailed appendices on methodology to supplement the discussion introducing chapters on each phase. It will be valuable, however, not only for its development of the morbidity sampling survey technique, but also for its general discussion of the difficult problem of disability due to chronic illness in an American industrial community. *J. Knowelden*

KAMAL, Ahmed Mohamed [D.P.H.], with the collaboration of M. S. E. ATTIA, M. A. FARID, G. A. MISSIH, W. OMAR, F. FIZK & M. O. SHOIB. **Epidemiology of Communicable Diseases.** pp. x + 567. 1958. Cairo: Anglo-Egyptian Bookshop.

In his introduction the author declares it his aim, together with his collaborators, to publish a book for students in Egypt dealing with the epidemiology of the important diseases of their own country. He writes with the authority of more than 15 years' experience of epidemiological work in the field, and his chapters are largely based on lectures which he has given for many years as Professor of Preventive Medicine at the Medical Faculty of Kasr-el-Ainy University, Cairo. In his opening chapter he defines epidemiology widely as the study of the ecology of diseases, both infectious and non-infectious. His object is the control, prevention and ultimate eradication of disease.

Early chapters deal with the theoretical aspects of the infectious process, with immunity and with the mechanism of epidemic spread of disease; the author then writes incisively on the practical methods of disinfection and disinfestation. Subsequent chapters describe the epidemiological features of specific diseases, and the closing chapters include an account of the international control of communicable diseases and most valuable advice on the legal powers of a Medical Officer

of Health and on the technique of epidemiological investigation.

With one exception these chapters, all of which are clear, concise and very readable, contain a wealth of information on local health problems. Only the chapter on the dysenteries fails to provide fully the information one would hope to find, and this is attributable to what is, in the reviewer's opinion, a grave defect in public health legislation, whereby "dysentery" is notifiable as such, and no attempt to differentiate between amoebiasis and shigellosis is required. Leptospirosis is not discussed and practically no information on venereal disease is given. Yaws and endemic syphilis gain no place, though these diseases may be too rare to merit inclusion. Since the author sets out to describe the ecology of disease, though the subject scarcely falls within the limits of the title chosen for the book, a chapter on child health and nutrition, so important to the welfare of the country, would have been a valuable addition.

A few interesting facts drawn from the wealth of information which is provided illustrate the public health problems which present themselves in Egypt. Poliomyelitis immunity, to all 3 types, is universally attained by the age of 5 years, all examples of the paralytic disease occurring in children below that age. Anthrax is an important zoonosis in Egypt, and Q fever is probably widespread. Typhoid fever is showing an increasing incidence in the country, the attack rate having risen from 338 per million in 1950 to 643 per million in 1955. The incidence in towns is 9–13 times as high as in rural communities. Urinary carriers of both *Salmonella typhi* and *Salm. paratyphi A* are more common than faecal carriers. With regard to shigella infections, investigations in a limited number of villages suggest that every member of the population is infected at least once annually, though adults rarely show overt disease. Limited surveys of village populations for amoebiasis have shown carrier rates of 60–97%, though there is no information as to what proportion were of the large race of *Entamoeba histolytica.*

In an admirable chapter on tuberculosis, Dr. M. Othman Shoib points out that, though the disease has been compulsorily notifiable since 1927, statistics are probably inaccurate. Careful surveys in 2 villages north of Cairo have shown incidences of active disease of 1·1 and 1·9%, which suggest that in the entire country there exist some 300,000 active and potentially infective tuberculous patients. Legislation has been passed for compulsory BCG inoculation, but it is not stated to what extent these powers have been exercised.

The book is well produced and clearly printed, typographical errors being remarkably few; considering that it is in a language foreign to the country the publishers merit much approbation. One important slip was noted in the chapter on cholera, where it is stated that, during the 1947 epidemic in Fayoum the incidence of the disease in those villages having a piped water supply was 66 per 100,000, while in the other villages (lacking a safe supply), it was 11.

The facts are presented without reserve and there is a complete absence of political bias. For instance, the author writes that, in the 1947 cholera epidemic, which was popularly supposed to have been introduced from India by British troops returning to the Canal Zone, he was able to prove that the disease had appeared simultaneously at several points on the Ismailia canal, "an act of sabotage no doubt", but he does not suggest who had done it.

Dr. Kamal is to be congratulated on the achievement of his object. He has produced a clear, instructive and authoritative text-book, which though bursting with information and up to date, should be readily assimilated by medical students and those training in Public Health in Egypt. *J. H. Walters*

INTERNATIONAL COMMITTEE ON BACTERIOLOGICAL NOMENCLATURE, Editorial Board [Edited by]. **International Code of Nomenclature of Bacteria and Viruses. Bacteriological Code.** pp. xxii + 186. 1958. Ames: Iowa State College Press, Iowa, U.S.A. [28s.]

The International Bacteriological Code of Nomenclature was approved at the Fourth International Congress of Microbiology in 1947 and was published in the Proceedings of that Congress, in the *Journal of Bacteriology*, 1948, v. 55, 287, and *Journal of General Microbiology*, 1949, v. 3, 444. This Code was translated into French, German, Spanish and Japanese, but the official version was (and remains) that published in the English language. Use of this Code indicated the need for change and clarification, and at the Sixth Congress (1953) the publication of a revised Code, together with annotations, was authorized. The revised Code was published in June 1958 with the title "International Code of Nomenclature of Bacteria and Viruses" and a short title of Bacteriological Code. The annotations are the work of R. E. BUCHANAN, and thus bear the stamp of this master of nomenclatural problems.

In the Bacteriological Code there are 4 chapters and 4 Appendices. Chapter 2 defines the Principles on which the Code is based, and the relations between bacteriological and botanical and zoological nomenclature. Scientific names of all taxonomic groups (taxa) are taken from Latin or Greek, or if from a modern language, are treated as if they were Latin. Nomenclature deals with (a) terms that denote categories of taxa (*e.g.* genus, species), and (b) names applied to individual units (*e.g. Bacillus subtilis, Streptococcus*). The word "name" and various modification (*e.g.* legitimate name, correct name) are defined in Principle 5. 15 categories of rank are listed in Principle 7, of which Genus, Species, Subspecies (variety) and Individual [Strain] are the most important to the working bacteriologist. Principle 8 lays down that a name is not intended to indicate the characters of a taxon but only to supply a means of referring to it. The well-known Principle of Priority (9), the use of nomenclatural types (11), and the admonition not to change the name of a taxon without serious motive (10), all support Principle 1 in its aim to keep nomenclature stable. Finally, Principle 12 lays down that a name has no standing in nomenclature unless it is validly published.

In Chapter 3 the Principles are turned into Rules, and the Rules are accompanied by Recommendations. The official part of this Chapter (*i.e.* the Rules, Recommendations and Notes) often reads like a legal

document but the Annotations come to the reader's rescue and by examples explain the more difficult passages. An attempt to summarize the Rules would lead to important omissions, but an idea of the ground covered can be had from the headings used for the different sections of Chapter 3. These deal with the names to be applied to taxa of different rank, the designation of nomenclatural types [this is important to authors who describe a new species], publication of names, citation of names of authors, changes in names of taxa, rejection and replacement of names, orthography and gender of names. [Authors of papers advocating a change in rank of an organism or its translation to another genus, or the creation of a new genus, and the editors of the journals to which their papers are submitted, should consult these Rules and Recommendations to see what the nomenclatural changes will be. Although the Recommendations do not have the strength of the Rules, they are a guide to good behaviour. There are certain practical difficulties. The Rules are retroactive, and the starting date for names is as early as 1753, long before any bacteria had been seen or isolated in pure culture. The effect of this is that Bizio's name *Serratia marcescens*, published in 1823, has to be considered as validly published, although the hemispherical capsules he saw by the crude microscope of his day, could not have been the small bacterium that (with yeasts) can produce bleeding polenta.]

Chapter 4 indicates the methods by which the Rules can legitimately be circumvented by appeal to a Judicial Commission. This Commission issues Official Opinions, some rejecting, some conserving particular names, and those issued up to June 1958 are given in Appendices C and D. [Opinions issued at the Seventh Congress, August 1958, have been published in the *International Bulletin of Bacteriological Nomenclature and Taxonomy*, October 1958.]

Appendix A deals with the transliteration of Greek words into Latin so that they can be used to form scientific names, and Appendix B recommends certain spellings.

[This Code is one of those reference works that is a must for every library that caters for the needs of bacteriologists. It does not define genera and species or solve any taxonomic problems, but it does stress the need for care and thought before changes, either in taxonomy or nomenclature, are suggested.]

S. T. Cowan

WALKER, Allan S. [M.D., Ch.M., F.R.A.C.P.] **Australia in the War of 1939–1945. Series 5. Medical. Vol. III. The Island Campaigns.** pp. xvi + 426, numerous illustrations. 1957. Canberra: Australian War Memorial. London: Angus & Robertson Ltd., 105, Great Russell Street, W.C.1. [35s.]

The third volume of the medical series of the Official History of Australia in the war of 1939–45 completes the account of the operational experiences of the Australian Army Medical Corps during this period. It commences in Papua in 1942 and details the long struggle to subdue tropical disease during almost 4 years of fighting in New Guinea, the Solomons and Borneo. Up to 1942 the experiences of the Army Medical Service were in countries distant from Australia; from that time onward came the struggle to overcome and prevent the dangers of infection in tropical countries nearer home.

In June 1942 FAIRLEY and MACKERRAS visited New Guinea and found the incidence of malaria in troops there disturbingly high despite suppressive quinine treatment, the total infection rate being estimated at about 45%. The position was complicated by the non-availability of plasmoquine to eradicate gametocyte carriers. Little destruction of adult mosquitoes was being attempted, and sprays and nets were an urgent requirement. Protective clothing was not being worn, repellents were not being used and the anti-malaria discipline of the New Guinea force was poor. They submitted plans for carrying out urgently needed protective measures, and warned that malaria itself was capable of deciding the issue of any military campaign in the South West Pacific.

On 26 August Japanese vessels arrived at Milne Bay and Australian troops were attacked there; severe fighting took place but ultimately the Japanese forces were defeated and withdrew. Later severe malarial casualties developed reaching 82 per 1,000 per week in early December, subsequently falling to 12 per 1,000 per week in February. In the Owen-Stanley campaign dysentery, malaria, pulmonary conditions, prickly heat and vitamin deficiencies proved very troublesome, during the retreat to Moresby. Subsequently when the force attacked again there was much trouble along the Kokoda trail—again with malaria and bacillary dysentery.

Largely through the advice of Lt.-Col. E. FORD sulphaguanidine became available at aid posts in September and medical officers gave it to all men with signs of clinical dysentery, 6 gm. at the first dose and 3 gm. repeated at 4-hour intervals along the route. Dysentery was controlled and ultimately stamped out; some say that sulphaguanidine saved Moresby.

The Japanese forces had both a high infection rate and a high death-rate from malaria. One Japanese medical officer stated that 10% of the men affected died and in one field hospital at Mambare 196 deaths were recorded, 80% being due to malaria. Apparently the Japanese had no standard or proven methods of treatment and individual medical officers followed their own ideas in therapy. Though there was much malaria among the Australian forces, there were practically no deaths. Throughout 1942 casualties from sickness in tropical areas were 5–30 times as common as battle casualties and malaria proved as great a menace as the Japanese.

In 1943, while warfare was static, a high standard of military hygiene and sanitation enabled casualties from malaria and other tropical diseases to be kept within reasonable limits, but once jungle fighting commenced effective prevention became most difficult. Thus in the Markham-Ramu and Huon Peninsula campaigns in New Guinea, out of a total force of 98,050 there were 47,534 medically sick, 28,909 being due to malaria. The battle casualties were only 3,140. The position was very serious and that year a Land

Headquarters Medical Research Unit was established in Northern Queensland to investigate the suppressive and causal prophylactic action of various anti-malarial drugs in experimentally infected military volunteers. During the investigations over 850 healthy volunteers were infected by mosquitoes conveying strains of *Plasmodium falciparum* or *P. vivax* or both from New Guinea and New Britain. It was soon found that quinine in a dosage of 10 grains daily completely failed to suppress malignant tertian malaria and a proportion of benign tertian infections as well. Sulphadiazine proved reasonably satisfactory in a dosage of 1·0 gm. daily in 17 out of 21 *P. falciparum* infections, but overt attacks of *P. vivax* malaria frequently occurred with this dosage. Similar results were obtained with sulphamerazine and sulphamezathine. With a correct mepacrine regime, however, it was found that *P. falciparum* infections were completely suppressed and radically cured, and *P. vivax* infections were suppressed over the period during which a dosage of 0·1 gm. daily was being taken. Febrile relapses of *P. vivax* malaria occurred some 2–7 weeks after the drug was stopped, but *P. falciparum* infections never relapsed, the disease having been completeiy cured.

A military conference was immediately called under the chairmanship of Lt.-General V. A. H. STURDEE, G.O.C. 1st Australian army. There was general agreement in view of these experimental results that the daily administration of 0·1 gm. mepacrine would prevent malaria breakdowns and lead to radical cure in *P. falciparum* infections and the complete suppression of *P. vivax* while the drug was being taken, though relapses might occur later. These measures subsequently led to the practical disappearance of *P. falciparum* infections and blackwater fever in the forces except in the case of a local outbreak in the Wewak area associated, at least in part, with irregular intake of mepacrine.

Mite-borne typhus reached its peak at the end of 1943 when anti-mite fluid, dibutyl phthalate, proved of great use in controlling its incidence. Infectious hepatitis and skin disorders were also troublesome.

Surgical aspects of the campaign were made very difficult at times by the heavy tropical rainfall, flooding and the mountainous nature of the country, but these difficulties were finally overcome and excellent surgical work followed. *N. Hamilton Fairley*

WIESINGER, Klaus. L'homme et son milieu. No. 1. L'homme et l'altitude. Physiologie et pathologie de l'altitude. **[Man and His Environment. No. I. Man and Altitude: the Physiological and Pathological Aspects]** 100 pp., 51 figs. (1 coloured on folding pl.) 1957. [Published also in German.] Basle 16: J. R. Geigy S.A., Switzerland.

The author of this book was the leading specialist in aviation medicine in Switzerland and was killed in an air crash in August, 1955. Fortunately, he had completed just before his death this article on the problems of physiology and pathology of altitude.

The object of the work was to provide a clear, concise account of the subject for the information of the medical profession generally. This aim has been accomplished in an admirable manner, and the problems dealt with should be crystal clear to those conversant with French or German. Unfortunately, there is no English translation.

There is nothing new in this book, which consists mainly of a review of the medical problems of altitude in flying and mountaineering culled from many sources, especially from the researches, publications and teachings of the American, British, French, German and other schools of aviation medicine. The script is very readable and the figures are excellent.

Only one aspect of aviation medicine is covered, namely, altitude. First, the characteristics of the different layers of the earth's atmosphere are dealt with. This is followed by a survey of the physiological effects of altitude on man in relation to his respiration, circulation, blood, metabolism, nervous system and psychology. Some pathological effects of altitude are discussed in a short chapter. Measures to overcome the ill-effects of high altitude are described: these include oxygen systems, pressure suits and pressurized cabins. Finally, there is a short chapter outlining some of the more important problems of man's travel into outer space. This is a good introduction to the study of the effects of altitude on man. *H. E. Whittingham*

HARGREAVES, G. R. **Psychiatry and the Public Health.** Heath Clark Lectures 1957. 118 pp. 1958. New York. Toronto. London: Oxford University Press, Amen House, Warwick Square, E.C.4. [12s. 6d.]

This is the published version of Professor Hargreaves's Heath Clark lectures of 1957. There are 5 separate lectures, each one self-contained but each forming a part in the story of Psychiatry and the Public Health.

The first lecture (*Psychiatry and its Origins*, pp. 1–23) traces the changes in attitude to mental health (or, more accurately, to mental illness). Explanations as to causes of mental illness are shown to be determined by the general body of knowledge at any given time. Some of the illogicalities of the present organization of psychiatric services are traced to their quite different origins; for example the services for the mentally ill, the mentally defective or the socially maladjusted. The difference between "care" and treatment has contributed to the failure to secure any comprehensive service.

The relation between mental health and the current patterns of accepted behaviour is stressed in the lecture on *Psychiatry and Society* (pp. 24–46). Behaviour held to be normal in one age or in one group may be abnormal and diagnostic of sickness in another. Psychiatric disorder may, in some instances, be no more than a departure from a socially determined norm, but this is not a wholly adequate concept, and some psychiatric disorder may be concealed by social influences. The belief that every culture pattern may in part determine the different types of psychiatric disorders which occur has stimulated not only psychiatrists but social and public health workers to re-examine their thinking.

Today a new problem faces the behavioural scientist, namely—the fact that environmental and social changes

have become so rapid that one generation may be unable to forecast the sort of world into which the next generation will grow up, and may therefore have little prospect of knowing how best to bring up children in a way appropriate to the future world in which they will be adult.

In the third lecture (*Psychiatry and Medical Administration*, pp. 47–71) administration is shown to have had much greater significance for the mentally sick than for the physically ill. In the past, treatment of the mentally ill was no more than removal from society; to private institutions or, for the poor, to prison. The guardians of *legal* rights were more involved than the guardians of *health*. The principles laid down by the 18th century reformers determined the administrative pattern applied later to the 19th century asylums and to the mental hospitals. Medical opinion was not invoked before the 19th century when a resident physician was required for the larger madhouse. By the end of the 19th century the strands of medical treatment and administration for the mentally ill had become inextricably interwoven but psychiatry had become isolated from general medicine and psychiatric and general hospitals were rigidly separated.

The whole administration of the asylum has become complex and clumsy because the purpose they now serve is so different from their original purpose. The many anomalies and conflicts arising out of this position have had an adverse effect upon the status of the psychiatrist in the mental hospital and have led some to believe that lay should replace medical administrators. Since the National Health Act there have been extensive and far reaching changes in the role of the mental hospital through the development of out-patient treatment and extra-mural psychiatry and the increase of voluntary hospital treatment. Mental health services for children have developed through education rather than health authorities and have had a separate and distinct history. Generally, the administrative organization of the various psychiatric services is not in accordance with the psychiatric needs of patients.

Lecture 4 is entitled *Psychiatry and the Family Doctor* (pp. 72–96). In the last 150 years there has been considerable psychiatric significance in the growing incapacity of the shrinking family to provide the emotional support that its members may need. The family itself has become increasingly isolated as an organism in society. It now falls to the state to provide the material support formerly undertaken by the extended family. While the state may be more effective in relieving such material distress, it cannot provide the emotional support formerly given by the large extended family. The changing role of the doctor in relation to the family is traced. At the turn of the century the genuine "family" doctor was available only to wealthy families. For others the doctor was more concerned with disease than with people. The psychiatrist today has been forced to recognize the impact upon the patient of his life in the family, and the relation between patient and family milieu. The family doctor of today should accept minor psychotherapy as an essential part of his role and should be trained to recognize those conditions for which specialist facilities are necessary.

Recent reports on the incidence of psychiatric conditions in general practice reveal the frequency and importance of anxiety states and endogenous depression. Since the family doctor has an important role to play in the diagnosis of each of these conditions and a different part to play in their treatment, the psychiatric education of the general practitioner should be appropriate. The practical problems of such teaching are discussed.

The final lecture deals with *Psychiatry and Public Health Practice* (pp. 97–118). Public Health was originally concerned with control of the external environment; water supply, sewage, housing etc. It is very doubtful whether action as specific, widespread and impersonal as was there possible, can ever be appropriate in the field of mental health. The health visitor is in the position of being able to contribute to the socio-psychological problems associated with maternity and child rearing. Her training at present does not adequately equip her to do so. The role of the health visitor must not be confused with that of the psychiatric social worker, who is a member of a team concerned with diagnosis and treatment of psychiatric disorder. Nevertheless, the psychiatric social worker might help in the training of the health visitor for her role of health counsellor and guide to the family through the normal emotional problems of maternity and childhood. There are many other occasions when the health visitor is ostensibly concerned with a physical health problem (perhaps of a child) but when the psychological implications may be far reaching and require considerable psychological insight.

The health services for schoolchildren could also extend more into the field of mental health through the public health worker acting as advisor and counsellor to the teacher.

The child guidance clinic should extend and broaden its interest and accept referrals from outside the school system. Such a child guidance service should be provided by the Regional Hospital Board and be integrated with similar services in general medicine, general psychiatry and so on.

In other instances, the boundaries between health services and education services are illogical and hinder development. The local health authority and the regional hospital board are sometimes organized in a way which leaves the mental patient in a no-man's-land with inadequate services for his rehabilitation and resettlement. The recommendations of the Royal Commission on the law relating to mental health have attacked this problem.

The new problems of public health require that new skills be developed. The new mental health worker should play an important part in the public health practice of the future. *Harry G. Maule*

SEGRETAIN, G., DROUHET, E. & MARIAT, F. Diagnostic de laboratoire en mycologie médicale. [**Laboratory Diagnosis in Medical Mycology**] 139 pp., 25 figs. 1958. St.-Mandé (Seine): Éditions de la Tourelle, 24, Rue de la République.

This little pocket volume written by three eminent mycologists forms part of a general series *Techniques*

de Base. It is an introduction to medical mycology designed to assist the microbiologist who is called upon to isolate and identify pathogenic fungi but who has had little or no previous experience of this group of organisms.

The first three chapters are devoted to a general introduction to the subject and include methods of diagnosis, the collection of suitable specimens, mycological techniques and the preparation of cultures. The mycoses are then divided into three main groups: (1) skin and mucosal infections which include pityriasis versicolor, erythrasma, piedra, the dermatophytoses and candidiasis; (2) the subcutaneous group consisting of sporotrichosis, chromoblastomycosis and mycetoma, and (3) the systemic group containing cryptococcosis, aspergillosis, histoplasmosis, coccidioidomycosis, North and South American blastomycosis, mucormycosis and cladosporosis. The causative fungi of the diseases in each of these groups are examined separately and the salient points in their isolation and specific identification are given. The size of the book necessitates that the descriptions be brief but this difficulty is overcome to a large extent by many excellent line drawings.

In the final chapter formulae of culture media and all the newer staining techniques are given. The whole is completed by a glossary. No difficulty should be experienced in reading the book for the authors have deliberately used a minimum of purely mycological terms and all of these are clearly defined.

Jacqueline Walker

Notice

Consideration has from time to time been given to the question whether it would be desirable to include authors' addresses in the headings of abstracts in the *Bulletins* and it has been decided that the additional time and cost involved would not be justified. Subscribers are advised, however, that the Bureau will, on request, notify them of the name and address of the author of the article, or the publisher of the journal, from which an abstract has been made.

The Bureau also deals with enquiries from individual subscribers relating to abstracts which have appeared in the *Bulletin of Hygiene* and the *Tropical Diseases Bulletin*; correct references and the exact nature of the information required should be stated.

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